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AN INTRODUCTION

TO

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AN

INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.

BY

T. HENRY GREEN, M.D. LOND.,

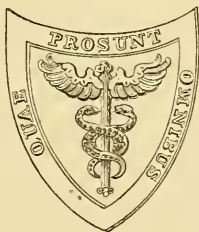
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AT CHARING CROSS HOSPITAL MEDICAL SCHOOL, ASSISTANT-
PHYSICIAN TO THE HOSPITAL FOR CONSUMPTION
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TO

WILSON FOX, M.D., F.R.S.,

PHYSICIAN EXTRAORDINARY TO HER MAJESTY THE QUEEN, PHYSICIAN IN ORDINARY
TO THEIR R. H.'S THE DUKE AND DUCHESS OF EDINBURGH, HOLME PROFESSOR
OF CLINICAL MEDICINE, FORMERLY PROFESSOR OF PATHOLOGICAL
ANATOMY AT UNIVERSITY COLLEGE, LONDON, AND
PHYSICIAN TO UNIVERSITY COLLEGE
HOSPITAL,

THIS SMALL WORK

Is Inscribed

WITH MUCH RESPECT AND GRATITUDE

BY HIS FORMER PUPIL,

THE AUTHOR.

PREFACE.

IN preparing the fifth edition of my Text-book of Pathology and Morbid Anatomy, I have again added much new matter, with the object of making the work a more complete guide for the student. All the chapters have been carefully revised, some alteration has been made in the arrangement of the work, and an addition has again been made to the number of wood-cuts. The new wood-cuts, as in previous editions, have been drawn by Mr. Collings from my own microscopical preparations.

T. HENRY GREEN.

74, WIMPOLE STREET, CAVENDISH SQUARE,

November, 1880.

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PATHOLOGY

AND

MORBID ANATOMY.

INTRODUCTION.

PATHOLOGY treats of the origin, nature, course, and causes of those changes in the body which constitute disease; *Morbid Anatomy* or *Morbid Histology*, of the actual alterations in the tissues which the disease has produced. The former is therefore comparable with Physiology, the latter with the Histology of the normal tissues.

By *disease* is understood some deviation from the state of health; a deviation consisting for the most part in an alteration in the functions, properties, or structure of some tissue or organ, owing to which its office in the economy is no longer performed in accordance with the normal standard.

Diseases are commonly divided into two classes—*organic* and *functional*. The former comprise all those which are attended by structural change; the latter those in which no such change is discoverable. Whether it be possible for the function of an organ or tissue to be abnormally performed quite irrespective of any alteration in its structure admits of some doubt. At all events, as our methods of minute investigation improve, and our knowledge of morbid histology increases, the class of functional diseases grows less; and although there still remain a large number of diseases in which we are unable to recognize any alteration of structure, and which must therefore still be described as functional, it is probable that all diseases will ultimately be found to be attended by more or less material change.

As *health* is itself merely a relative term and implies no definite performance of the processes of life, so *disease* is equally indefinite;

it cannot be separated from health by any well-defined boundary, the one passing by insensible gradations into the other.

Disease is thus, in most cases, an abnormal performance of those processes which constitute life, and a knowledge of these processes must therefore necessarily precede the study of pathology. Life comprises the formation and maintenance of the tissues and the exhibition of their various functions. Such formation and maintenance, which may be included under the general term of *Nutrition*, consist in the continuous supply of new material, the separation of this from the blood and its appropriation by the tissues, together with the removal of the products of their waste. *Function* is the special manifestation of the life of the part, as distinct from its growth and the maintenance of its structure; in the secreting cell, consisting in the alteration of the substances abstracted from the blood to fulfil some special purpose in the economy; in nerve, in the transmission of impulses of motion and sensation, etc. The performance of function is obviously dependent upon the state of nutrition. When both of these are normal the condition is one of *health*, when abnormal one of *disease*.

As in health the nutrition is principally dependent upon the solid tissues, these abstracting, appropriating, and altering the material which is supplied to them by the blood; so in most forms of disease it is these tissues which play the more important part, and alterations in them are amongst the most frequent of the morbid processes.

The supply and composition of the blood must obviously at the same time constitute most important factors in disease. Owing to the intimate relation which subsists between the blood and the solid tissues, any alteration in the supply or composition of the former must exercise more or less influence upon the nutritive processes. In regarding the blood, however, as an element in the causation of disease, it must be borne in mind that this fluid is in a state of constant dependence upon other parts; its component elements are derived from external sources and undergo continual change, and although possibly under certain circumstances it may become altered by virtue of changes in the nutritive activity of its cellular elements, alterations in its constitution must in most cases result either from some change in the process of its formation, as from the ingestion of improper or insufficient food, mal-assimilation, or disease of the lymphatic structures; from changes in the secretory or excretory processes; or from the introduction of foreign substances, derived from extraneous sources. Whilst, there-

fore, alterations in the composition of the blood may be important agents in the production of diseased processes in other tissues, such alterations are in most cases secondary to some abnormality in its formation or depuration, or to its contamination by substances derived from without. Owing to the facility with which it becomes the recipient of foreign substances, it is often the first tissue to become altered, and it not infrequently constitutes the principal seat of the diseased process. This is the case, for example, in many of those diseases which owe their origin to the introduction of minute organisms, as the contagious fevers.

The blood may also play an important part in disease owing to its white corpuscles passing through the walls of the bloodvessels into the surrounding tissues. This occurs in the process of inflammation, and probably also in the development of many of the new formations.

Lastly, the influence of the nervous system must be taken into account in considering abnormal conditions of nutrition and function. This, by regulating the circulation and supply of blood, must to a certain extent control tissue-change. The results of experimental and clinical observation render it exceedingly probable that many nerves also contain fibres which exercise a direct influence upon nutrition, independently of that which is due to their vaso-motor filaments. In support of this view may be adduced the well-known observations of Ludwig and Heidenhain on the influence of the chorda tympani upon the secretion of the submaxillary gland, which prove that the increased secretion which results from the stimulation of this nerve is due to an increased activity of the secreting elements of the gland and not to changes in the bloodvessels. Recent histological researches, also, which are tending to show that nerve-fibres terminate in the ultimate elements of nearly all tissues, and the fact that rapid atrophy of muscles follows lesions of certain portions of the nervous centres and many injuries of the nerve-trunks, render it exceedingly probable that the nutrition of muscle and glandular organs, if not of many other parts, is more or less under the *direct* influence of the nervous system.

The *first* part of this work will be devoted exclusively to the consideration of morbid processes which are characterized mainly by alterations in nutrition; the *second*, to changes in the blood and circulation; and the *third*, to the process of inflammation. In considering the several morbid processes, the general pathology of each process will first be described, and subsequently the same process as it occurs in the different organs and tissues.

CHAPTER I.

THE CELL.

As the most important element in nutrition, both in health and disease, is the activity of the tissues themselves—the supply of nutritive material, although an essential, being merely a *passive* part of the process—it becomes necessary to consider, somewhat minutely, those parts of the tissues in which this activity resides.

Ever since Schwann discovered the cellular nature of animals, and established the analogy between animal and vegetable cells, there has been a gradually increasing conviction amongst physiologists, which has now become an universally accepted physiological and pathological doctrine, that the *cell* is the seat of nutrition and function; and further, that *each individual cell* is itself an independent organism, endowed with those properties, and capable of exhibiting those active changes which are characteristic of life. Every organized part of the body is either cellular or is derived from cells, and the cells themselves originate from pre-existing cells, and under no circumstances do they originate *de novo*.

Whilst therefore the whole body is made up of cells, or of substances derived from cells, and the cell is itself the ultimate morphological element which is capable of exhibiting manifestations of life, it must be borne in mind that in a complex organism, the phenomena of life are the result of the combined activity of innumerable cells, many of which possess distinct and peculiar functions, and that by their combination they become endowed with new powers, and exhibit new forces, so that although each individual unit possesses an independent activity, it is in a state of constant dependence upon others with which it is more or less intimately associated.

CONSTITUTION OF CELLS.—When the analogy was established between the animal and vegetable cells, the former was held to be constructed in all cases upon the same principle as the latter, and to consist of a *cell-wall*, inclosing a cavity, in which were contained a *nucleus* and *fluid contents* (Fig. 1). This was the idea of the cell held by Schwann and Remak, and supported especially by Vir-

chow, who maintained that these three constituents were essential to its vitality and existence.

During recent years, however, this definition has been modified. The existence of a cell-wall was in many cases not evident. In embryonic cells, in those of many rapidly growing new formations, and in the cells of blood, pus, and mucus, no limiting membrane could be demonstrated. This led to a new definition of the cell by Leydig and Max Schultze, who held that a little mass of matter inclosing a nucleus was all that was necessary for its constitution. The latter of these physiologists not only rejected the cell-wall as an essential constituent, but established the identity of the mass of matter (cell-contents) with animal sarcode—a contractile substance existing in the lower animals—and showed that, like it, it was endowed with the power of spontaneous movement. This substance he called *protoplasm*. He further pointed out, that the existence of a distinct cell-wall was the result of a retrograde process taking place in the outer layers of the protoplasm, and that the latter was the real seat of the activity of the cell. These views closely correspond with those held by Dr. Beale in this country.¹

The definition of a cell has been still further modified by Brücke, Stricker, and others, who consider that the existence of a nucleus is not essential to its constitution. This opinion is principally based upon the fact, that in the cryptogamia, and in some of the lowest animal forms, cells occur in which no nucleus is visible.

It would thus appear probable that a simple mass of protoplasm may, in some exceptional cases, be all that is necessary to constitute a cell—*i. e.*, an elementary organism, capable of exhibiting independently all the phenomena of life; but that the nucleus is an exceedingly constant and almost invariable constituent. The cell-wall is much less constant, and being the result of a retrograde change in the outer layers of the protoplasm, it must be regarded, in point of vitality, as inferior to the rest of the cell.

Protoplasm itself is an unstable albuminoid compound, which is insoluble in water and coagulates at death. As usually met with, it

FIG. 1.



Cells from a cancer. Showing cell-wall, cell-contents, nuclei, and nucleoli. The nuclei dividing.

¹ Dr. Beale calls the protoplasm, *germinal matter* or *bioplasm*; the cell-wall *formed material*.

is a homogeneous structureless material, of a soft and viscid consistence. In consistence, however, it is subject to variations, being sometimes perfectly fluid, at others more or less solid and gelatinous. In old cells it often becomes transformed, by the loss of water, into a more solid albuminoid substance—*keratin*. This occurs in the epidermis and nail. Protoplasm may also become gradually converted into other modifications of the protein group—into mucin, globulin, hæmoglobin, etc. The cell-wall, when it exists, is of much firmer consistence than the protoplasm. In some cells the protoplasm constitutes but a small proportion of the body of the cell, other substances, which are either the result of its metamorphosis, or have been taken up from without, being associated with it. Thus fat is met with in the cells of adipose tissue, and of the liver. (See Fig. 6.) Pigment, calcareous particles, pepsin, etc., are also met with in cells.

The *nucleus* is more constant both in size and form than the cell. It is usually spherical or oval in shape, and often contains one or more minute round or angular bodies, termed *nucleoli*. It offers a greater resistance to chemical reagents than the other constituents of the cell, and is also stained more deeply by carmine.

The original form of the nucleus is vesicular. In the earliest cells of embryonic tissue it possesses a delicate membrane inclosing a nucleolus and fluid contents, thus resembling in its structure the cell. Subsequently, however, it loses its vesicular character, and as usually met with it is a solid perfectly homogeneous, or faintly granular body, in which the nucleolus is still visible. The recognition of the nucleus is not always possible, owing to its presence being obscured by fat, pigment, or other substances contained within the cell. (See Fig. 28.) In some cells the nuclei gradually disappear. The colored blood-cells and the cells of the superficial layers of the epidermis are examples of cells in which the original nucleus has become lost. Lastly, it must be mentioned, that several nuclei may be contained within the same cell. (See Fig. 2.)

PHYSIOLOGY OF CELLS.—The cell, as already stated, is capable of absorbing and transforming matter, of excretion, and of growth. It is also endowed with the power of changing its form, of cohering with other cells, of undergoing more or less active movement, and of reproduction. The nature of the processes which occur within cells during these various manifestations of their vitality is, for the most part, involved in obscurity; we know little more than what is supplied to them and what is excreted. The question now arises as to what

part is played by the respective constituents of cells—whether the cell-wall, the body of the cell (protoplasm), and the nucleus have different offices.

The cell-wall, being the result of a retrogressive change in the protoplasm, cannot be regarded as taking any part in the life of the cell, the activity of which is much diminished by its existence, as is also its power of reproducing itself by simple division. It is in old cells that a cell-wall is most frequently met with; in those newly formed it is entirely wanting.

The nucleus has usually been looked upon as the seat of the nutrition, as distinct from the specific functions of cells, and has been supposed to play an important part in their multiplication and reproduction. The fact that when a cell divides, the division usually commences in the nucleus, and only subsequently takes place in the rest of the cell, would appear to favor this view; as would also the great uniformity of the nucleus both in size and form, whatever be the functional nature of the cell. It must be borne in mind, however, that non-nucleated cells may multiply, and that nucleated cells have been observed to divide, the nucleus itself taking no part in the process.

Whatever be the part played by the nucleus, there can be no doubt that the protoplasm is the most important factor of the cell, and it may itself be the only constituent. The spontaneous movements, alterations in form, and migratory powers characteristic of young cells, are due to the protoplasm. Such movements are observed in the cells of the embryo, in lymphoid and young epithelial cells, in some of the cells of connective tissue, and in white blood and pus cells.

The protoplasm, as already stated, may be the sole seat of the nutritive and formative power of the cell. It would appear, however, probable that it is more especially concerned in the performance of function, and that the specific functional peculiarities of cells are dependent rather upon it than upon their other constituents. The volume and consistence of the protoplasm vary in different cells, and in the same cell, at different times and under different circumstances. It is apparently capable of imbibing and giving up fluids, at the same time undergoing corresponding alterations in volume. These considerations render it probable that it is the seat of the selective power of the cell, and of those other properties which represent its specific functions.

GENESIS OF CELLS.—The proposition of Virchow, that every cell originates directly from a pre-existing cell, forms the basis of the

pathology of the present day. To Remak, however, must be ascribed the merit of having first established the cellular origin of the tissues.

The multiplication of cells may take place in three ways—by *simple division*, by *gemmation*, and by *endogenous growth*. In the first two methods the cell breaks up into fragments; in the last, new cells originate within the parent cell. The process is obviously associated with growth and increase of the protoplasm.

The multiplication by simple division is the most frequent method. The cell divides and forms two cells, and each of these again divides

and forms two more, and so on. In nucleated cells the nucleus as a rule divides first. The nucleus, however, may divide and multiply within the cell without any division of the cell taking place. If the nuclei multiply within the cell, and the protoplasm continuously increase without subsequent division of the cell taking place, large, many-nucleated, irregular-shaped masses of protoplasm are produced. These are the giant or myeloid cells, which are met with in the medulla of young bone, in some new formations, and in certain inflammatory growths. (Fig. 2.) (See also "Myeloid Sarcoma," Fig.

FIG. 2.



A Multinucleated Cell. From the lung in a case of chronic phthisis. Showing the large number of nuclei with bright nucleoli. $\times 400$.

51.) The existence of a dense cell-wall interferes with the process of multiplication by simple division.

By endogenous multiplication is understood the development of cells within pre-existing cells. The multiplication of the cells of cartilage, such as occurs in the growth of bone and in the process of inflammation, has been adduced as an example of this mode of cell formation. Here, however, we have simply the division of the cartilage cell within its capsule, and the process is precisely similar to multiplication by simple division (see Fig. 96, *d*). The mode of cell formation which must be regarded as strictly endogenous, is what is now commonly known as *Vacuolation*. This was described some time ago by Virchow in his "Cellular Pathology;" and owing to the more recent researches of Klein and others, it now occupies an important place in the history of cell development. The process consists in the

formation of a vacuole in the body of the cell. This vacuole may gradually increase in size until it occupies nearly the whole of the cell, being merely surrounded by a thin layer of protoplasm, in which may often be seen the displaced nucleus (Fig. 3, *b*). Within this vacuole one or more new elements are formed. These either originate from the nucleus of the cell, or they are produced from the protoplasm which forms the wall of the vacuole. In the latter case, according to Dr. Klein, buds grow out from the protoplasmic wall towards the interior of the vacuole, and these becoming detached form new cells.¹ A vacuolated cell with an endogenous brood is shown in the accompanying drawing (Fig. 3), for which I am indebted to the observer just quoted. It must, however, be remembered, in forming any conclusion as to the origin of small cells within a larger cell, that there exists the possibility that these may have entered from without.

The endogenous mode of cell formation is not that by which tissues regenerate themselves. This is usually effected by simple division. Elements which have an endogenous origin have commonly a destiny different from that of the parent cell.

In multiplication by gemmation, a small portion of the protoplasm projects from the cell and becomes detached by constriction at its base, thus forming a new cell. This is much less frequent than the two former processes.²

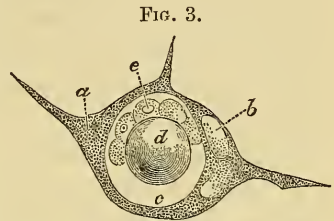


FIG. 3.
A Vacuolated Cell. *a.* Protoplasm of cell constituting wall of the vacuole. *b.* Displaced nuclei. *c.* The vacuole. *d.* Drop of fat. *e.* Endogenous brood. (Klein.)

¹ "The Anatomy of the Lymphatic System," vol. i. pp. 55-60; and Klein on "Endothelial vesicles of growing bloodvessels in the embryo chick." "Sitzungsberichte der Wiener k. Academie d. Wissenschaften," Part for March, 1871.

² The author wishes it to be distinctly understood, that in the subsequent pages the term "cell" is employed to designate the most elementary factor of the tissues which is capable of exhibiting the phenomena characteristic of an independent organism, quite irrespectively of the existence of a cell-wall, or even of a nucleus.

CHAPTER II.

NUTRITION ARRESTED.

Necrosis.

THE absolute and permanent arrest of nutrition in a part constitutes necrosis, gangrene, or local death.

ETIOLOGY.—Whatever interferes with the supply of nutritive material to a part, or destroys the activity of its cellular elements, may cause its death.

A. The supply of nutritive material may be interfered with by:—

1. *Obstruction in the Arteries.*—This is a common cause of necrosis. The obstruction may be caused by a ligature, by compression of the vessel, by solution of its continuity, by thrombosis or embolism, and by disease of the arterial coats. If the obstruction be complete and a collateral circulation cannot be established, death of the part quickly ensues.

2. *Obstruction in the Capillaries.*—Obstruction here is often the result of pressure upon or stretching of the vessels. This may take place from the accumulation of inflammatory products, hemorrhage, or from the pressure exercised by new growths. The resulting obstruction to the capillary circulation causes the death of the immediately adjacent tissues. As examples of necrosis from this cause may be mentioned that of the superficial layers of the bone which so frequently results from periostitis, owing to the compression of the capillaries between the cone and the periosteum; also the sloughing of the skin over a quickly-growing abscess.

The capillary circulation is also obstructed in conditions of complete stasis—*i. e.*, stoppage of the blood-stream with coagulation of the blood. Such stasis, which occurs as the result of necrosis of the capillary walls from whatever cause, will be considered in the chapters on Inflammation and Thrombosis. It will be sufficient to note here that its occurrence may not only be a cause of tissue disorganization, but that necrotic processes by destroying the vitality of the capillary walls may induce stasis. It is stasis thus produced which tends to prevent hemorrhage from gangrenous parts.

3. *Obstruction in the Veins.*—Obstruction to the return of blood by the veins must be so complete in order to arrest nutrition that it is in itself rarely a cause of necrosis. It is when associated with obstruction in the arteries that it constitutes an important agent in producing this result. This combination of venous and arterial obstruction is seen in a strangulated hernia, in the invagination of a portion of the intestine, in the constriction of a part by a tight bandage, in contusions and lacerations of the soft parts in which both arteries and veins are injured or become strangulated by the tension of the tissues which subsequently ensues.

4. *Diminished Cardiac Power.*—This is never independently a cause of necrosis. In cases, however, of excessive general debility, or disease of the cardiac substance, the consequent diminution in the contractile power of the heart materially aids the foregoing causes in producing a fatal blood-stasis. The arrest of the circulation in “senile gangrene,” and that which so often occurs in the tissues of the back in adynamic fevers and in chronic exhausting diseases, is in part the result of diminished cardiac power. This arrest in the last-named conditions, is usually determined by some injurious stimulation of the tissue—in other words, it is a part of an inflammatory process.

5. *Inflammation.*—The effect of the inflammatory process is to impede or arrest the circulation, and to impair the vitality of the affected part, and the intensity of the process may be so great as to permanently arrest the circulation and cause death (see “Inflammation”). Certain inflammations have a special tendency to terminate in necrosis, as diphtheria, carbuncle, and “hospital gangrene.” In these conditions the necrotic tendency is probably due to the presence of minute organisms. In all cases, the more impaired the nutrition of the part which becomes the seat of an inflammatory process, the more likely is this to cause its death.

B. Destruction of the activity of the cellular elements may be caused by:—

1. *Traumatic and Chemical Agencies.*—A part may be completely disorganized and lose its vitality as the result of external violence. Many corrosive substances also, as acids and caustic alkalies, destroy the life of cells. The cells of a tissue may thus have their vitality destroyed, and the bloodvessels remain uninjured, or both cells and vessels may be involved. Putrid organic substances, as foul urine and secretions from wounds, may in the same way interfere with the life of cells, and cause their death. They most frequently do so,

however, by inducing in the first place an inflammatory process ; but sometimes death ensues directly, quite independently of inflammation. The injurious influence of such liquids is probably due to the presence in them of minute organisms (septic bacteria).

2. *Abnormal Temperature.*—The vitality of cells can only be maintained within certain limits of temperature ; extreme degrees of heat or cold cause their death. Here, as in the case of other injuries, the abnormal temperature often, but by no means always, causes in the first place an inflammatory process.

Having considered the several causes of necrosis, it must be borne in mind that the process is often complex and due to the combined influence of two or more of them. The liability to necrosis will also depend greatly upon *the power of the tissues to resist necrotic influences*. Conditions which would lead to the death of a part in which circulation was already impeded or the vitality of the cellular elements impaired, would produce no such effect where such local weakness did not obtain. This is well exemplified by the necrosis of the tissues of the back from pressure, which so often occurs in conditions of debility ; by the gangrene of the extremities which sometimes results from the long continued ingestion of ergot ; and especially by senile gangrene.

Senile Gangrene.—This is a form of necrosis which affects especially the lower extremities of old people, and is the result of several of those etiological conditions which have already been enumerated.

The most important element in the production of senile gangrene consists in the occurrence of atheromatous or calcareous changes in the arteries of the limb, in consequence of which the circulation in it becomes impeded and its vitality impaired. This is evidenced by the coldness of the feet, the cramps, and the other abnormal sensations which are so often experienced by the patient some time before the gangrene sets in. This tendency to local stagnation of the circulation is usually materially increased by the simultaneous atrophy or degeneration of the muscular substance of the heart itself. The combined effect of the diminished *vis à tergo* and of the arterial degeneration may, in some cases, be alone sufficient to cause arrest of the circulation and the formation of thrombi in the vessels of the limb, and thus to cause gangrene. The supervention of the gangrene, however, is usually determined by some injurious stimulation of the tissue, as a slight abrasion of the foot, a bruise, injury to a corn, or excess of heat or cold, which sets up inflammation in the already weakened

part, and thus by still further obstructing the circulation in it, and impairing its vitality, causes its death.

CHARACTERS OF DEAD PART.—The characters of the dead part vary with its structure, its vascularity, the cause of the necrosis, the acuteness of the process, and the possibility of the access of atmospheric air. The more vascular the tissue, the softer its structure, and the more it is exposed to the atmosphere, the more rapidly and completely does it undergo decomposition. Bone, cartilage, and tendons, which are firm hard tissues, containing comparatively but few vessels, undergo very little alteration in structure and form; whereas softer parts are much more rapidly and completely destroyed.

In those cases in which the dead part contains but little water, as when the necrotic process is associated with obstruction of the arteries and there is no interference with absorption by the veins and lymphatics, or when, owing to the destruction of the epidermis, there is great loss of water by evaporation, it may gradually dry up and become converted into a dark shrunken mass which undergoes but little further change. This constitutes *dry gangrene* or *mummification*. It often occurs in necrosis from embolism, in that induced by ergot of rye, and in senile gangrene.

When, on the other hand, the part is moist, as where the necrosis is associated with venous obstruction, so that the return of blood and absorption of fluids is interfered with, the gradual drying up of the dead tissue rarely takes place. Under these circumstances, if the part be exposed to atmospheric influences, septic bacteria obtain an entrance, and the moisture being favorable to their development, the dead tissue undergoes putrid decomposition, such as occurs naturally in the body after death. In a limb, for example, the liquor sanguinis transudes from the bloodvessels, and, evaporation being to a great extent hindered by the epidermis, the transuded and accumulated liquids often form large bullæ on the surface. As decomposition proceeds, gases are generated in the part—principally sulphuretted hydrogen, ammonia, nitrogen, and carbonic acid. These give rise to the emphysematous crackling which is so often associated with the gangrenous process. The tissues at the same time undergo a process of softening or liquefaction, the limb becomes exceedingly offensive, and owing to alterations in the transuded hæmoglobin, changes from a reddish color to a brownish or greenish black. This form of necrosis is known as *moist gangrene*. It occurs only in external parts and in those internal organs to which the air is freely accessible, as the lungs.

When met with in other situations it is due to infection with septic matter.

In many cases the necrotic process is associated with fatty degeneration. The dead tissue then presents somewhat different characters, often becoming *caseous* or *liquefying*. These forms will be considered in the chapters devoted to this form of degeneration.

The changes in certain tissues must now be considered more particularly. Firstly, with regard to the blood: This fluid undergoes the earliest and most rapid change. The hæmoglobin escapes from the red corpuscles, partly by exudation, and partly by the destruction of the corpuscles themselves, and dissolved in the liquor sanguinis permeates the surrounding tissues. The corpuscles are ultimately completely annihilated, nothing remaining but a few minute granules. The staining of the tissues with hæmoglobin is commonly known as *post mortem staining*, and the appearances it presents are very characteristic. The lining membrane of the heart and bloodvessels, being in immediate contact with the blood after death, are the parts principally affected. The staining is of an uniform pinkish-red color, thus differing from the punctiform and stratiform redness of hyperæmia from which it must be carefully distinguished. The amount of staining is in proportion to the rapidity with which decomposition has taken place, and to the amount of blood contained in the part at the time of death.

In muscle the arrest of nutrition is accompanied by a state of rigidity, known as the *Rigor Mortis*. This is a peculiar condition of the muscles observed in almost all bodies after death, in which they become firm and somewhat shortened, as though in a state of chronic contraction. It comes on as soon as the muscles have lost their irritability—*i. e.*, their capability of responding to artificial stimulation; in other words, as soon as the nutritive processes have completely ceased. The time of its appearance will therefore depend upon the state of nutrition of the muscles at the time of death; the more healthy and vigorous this is, the longer it is before the nutritive processes completely cease, and consequently the longer it is before the rigor mortis supervenes. The length of its duration and its intensity are in direct proportion to the lateness of its appearance. In people, for example, who are in perfect health, and die suddenly, as from accident, the rigor mortis does not usually come on until from ten to twenty-four hours after death; it is very marked, and often lasts two or three days. In those, on the other hand, who die from some exhausting disease, as from

chronic phthisis or the adynamic fevers, in which the nutrition of the muscles becomes much impaired, the rigor mortis appears very soon, sometimes as early as ten minutes after death; it is very slight, and may pass off in less than an hour. It has been said that in cases of death from poisoning by carbonic acid and sulphuretted hydrogen, from lightning, and from some of the severer forms of the adynamic fevers, the rigor mortis is entirely absent. It is doubtful, however, if this is the case, as the rigor mortis has probably escaped observation, owing to its early supervention and rapid disappearance. As soon as the rigor mortis has passed off decomposition of the muscular tissue commences.

With regard to the nature of the change—it was formerly supposed to be a spontaneous contraction, the last act of vitality on the part of the muscle. More recently, however, Kühne and others have shown that it is really owing to the coagulation of the albuminous substance of the muscle—myosin. The myosin, fluid during life, coagulates when nutrition has ceased, the coagulation being attended by the liberation of a free acid. Thus is produced the firmness, hardness, and opacity of the muscle, which disappear as soon as disintegration and decomposition commence. The transverse striation of the fibres then becomes indistinct, and gives place to irregular rows of granules and fat molecules, the muscle softens, its sarcolemma is destroyed, and ultimately nothing remains but a soft structureless débris. This change occurs not only in muscle, but in the cells of other tissues a similar coagulation of the protoplasm takes place on the cessation of the nutritive processes.

Respecting the changes in other tissues—protoplasm generally not only coagulates but tends to become finely granular after death. It sometimes increases in size so that the cells look swollen; and in nucleated cells the nucleus often shrinks or entirely disappears. The cells ultimately break up into molecules of various sizes. In adipose tissue, the cells diminish in size, owing to the escape of the fluid fat which diffuses itself throughout the surrounding structures. The fibres of connective tissue swell up, become opaque, and ultimately liquefy. In nerve-fibres, the white substance of Schwann coagulates and collects into small drops (myelin) with the neurilemma. Cartilage and bone resist the necrotizing process longer than any of the tissues and are the least altered by it.

TERMINATIONS.—The termination of the necrotic process varies. It may, after involving a greater or less extent of tissue, become

arrested, and a "line of demarcation" form between the dead and living parts—*Circumscribed Gangrene*; or the process may continue to extend without any such attempt at recovery—*Diffuse Gangrene*. Whether the one or the other occurs will depend, in great measure, upon the presence or absence of any pre-existing local weakness either in the circulation or the tissues. Necrotic processes in a healthy individual tend to become circumscribed, but when the circulation is enfeebled, or the vitality of the tissues impaired, as in the aged, they are liable to be diffuse. (See "Senile Gangrene.") The presence of septic bacteria also tends to interfere with the arrest of a necrotic process.

When the process becomes arrested, the dead tissue—the sphacelus or slough—acts as a foreign body, and as such sets up inflammatory changes in the adjacent living structures, and by this means it is ultimately removed or becomes encapsuled. The tissues immediately surrounding the necrosed part are thus in a state of inflammation, as is evidenced in external structures by their swelled condition, red color, and high temperature. As the necrotic process ceases, the dead fragment becomes limited by this line of inflamed tissue, which constitutes the "*line of demarcation*" between the dead and living parts. Along this line a process of suppuration takes place, and by means of this the dead mass is gradually separated from the surrounding structures. The ultimate termination of the process depends principally upon the situation of the affected part—if this be superficial, the slough is thrown off, as in external parts, the intestines, the pharynx, etc., an ulcerated surface being left. If the dead mass is deeply seated, its removal becomes possible only by the extension of the necrotizing process to the surface, as is exemplified by the spontaneous removal of necrosed bone through fistulous openings in the soft parts.

In other cases the inflammatory process which takes place in the tissues surrounding the dead part is less intense, and the formation of pus is less abundant and is soon followed by that of vascularized connective tissue, a layer of which is ultimately formed around the necrosed mass, by which it becomes *encapsuled*. This occurs especially in internal parts. Examples of it are furnished by foreign bodies, hemorrhagic infarcts, accumulated epithelial products, portions of necrosed bone, and a foetus in the abdominal cavity, all of which may thus become surrounded by a layer of connective tissue. The

part when thus encapsuled is usually rendered inert and no longer acts as an irritant to the tissues in which it lies; it undergoes a gradual process of absorption and drying up, and often becomes calcified.

CHAPTER III.

NUTRITION IMPAIRED.

It has been seen in the preceding chapter that the absolute arrest of nutrition is followed by the complete cessation of all manifestations of vitality and function, constituting necrosis or local death. Those conditions must now be considered in which the interference with nutrition, for the most part, falls short of absolute arrest, and in which, although vitality is impaired, death is only an occasional sequence. Such conditions are comprised under "Atrophy," and "Degeneration."

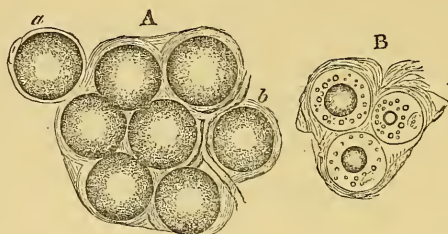
Atrophy.

Atrophy is a diminution in the amount of a tissue, owing either to diminution in the *size*, or diminution in the *number*, of the histological elements of which it is composed. It is attended by loss of weight, and impairment of function. When the elements are diminished in *size* only, it is called *Simple Atrophy*; when the *number* is diminished, it is called *Numerical Atrophy*. These two varieties are often associated, being different stages of the same process.

Simple diminution in the size of the elements of a tissue is the most common condition met with in atrophy. It is well exemplified by what takes place in ordinary emaciation, in which the fat gradually disappears from the subcutaneous adipose tissue. Adipose tissue is merely common connective tissue, many cells of which are distended with fat. When a person emaciates, the fat is gradually removed from the cells so that they diminish in size, and the fat which completely filled the cell may be reduced to a few isolated drops; the cell-wall and nucleus at the same time often become distinctly visible

(Fig. 4). Here there is no destruction of the cells, no diminution in their number, but simply the removal of some of their contents.

FIG. 4.



Adipose tissue. A. Normal. B. Atrophic, from a case of phthisis. a. A single fat-cell, with cell-wall, nucleus, and drop of fat. $\times 300$. (Virchow.)

As the fat is removed from the cells it is usually partially replaced by a serous fluid. A multiplication of the nucleus is also often observed.

This diminution in the size of the elements may take place in any tissue. The cells of all glandular organs may thus become atrophied, and so produce a diminution in the size of the whole organ. Muscular tissue in the same way atrophies by the diminution in the size of its primitive fasciculi; and here also, as in adipose tissue, the process appears often to be associated with a multiplication of the nuclei of the muscle. In all these cases the elements remain almost unchanged, and hence all that is necessary for the restitution of the tissue is an increase in their nutritive activity, and the assimilation of more material.

A diminution in the number of elements—numerical atrophy—is often an advanced stage of the more simple process. The elements not only diminish in size, but some of them actually perish and cease to exist as vital agents. This destruction of histological elements which occurs both in atrophy and in some forms of degeneration has been called by Virchow *Necrobiosis*. In it, restitution is only possible by the production of new elements, whereas in simple atrophy repair can be effected without new formation. In certain tissues, as the spleen, lymphatic glands, and skin, atrophy is probably always due mainly to numerical loss.

Atrophy may be *general*—affecting to a greater or less extent all the organs and tissues of the body, or it may be *partial* and limited to particular parts. General atrophy affects in the first place the subcutaneous adipose tissue, then the adipose tissue in other situa-

tions, as that surrounding the viscera and in the omentum, then the muscles and glandular organs, and lastly the nervous and osseous structures.

Although atrophy in its strict signification consists simply in a diminution in the size or in the number of the component elements of a tissue, it is rarely a perfectly simple process, but is usually associated with more or less *fatty degeneration*. This is owing to the fact that whenever the nutrition of a part is so much interfered with as to cause it to atrophy, it is very prone to undergo fatty changes; and it will be seen, when speaking of "fatty degeneration," that this process owes its origin to causes similar to those which produce atrophy itself.

ETIOLOGY.—In speaking of the causes of atrophy, it will be necessary to distinguish between those which act upon the tissues generally, and those which have merely a local influence.

General Atrophy may be caused by:—

1. *Deficient Supply of Nutritive Material*.—Whatever interferes with the supply of nutritive material to the tissues will be followed by their atrophy. Deficient supply of food; obstruction to the passage of the food into the stomach or intestines, as in stricture of the œsophagus or pylorus; the mal-assimilation which results from the various conditions giving rise to dyspepsia; interference with the absorption of the chyle, from obstruction of the thoracic duct, or disease of the mesenteric glands constituting the so-called "tabes mesenterica;" may all in this manner be causes of general atrophy.

2. *Excessive Waste*.—All those conditions which are attended by the loss of large quantities of nutritive material may be causes of general atrophy. Such conditions are furnished by continuous hemorrhages, profuse and long-continued suppuration such as often occurs in caries and empyema, diarrhœa, and the excretion of large quantities of albumen or sugar as in Bright's disease or diabetes. The waste resulting from the increased tissue-change which accompanies acute febrile diseases must also be included under this head.

3. *Impaired Nutritive Activity*.—This constitutes an important element in the production of the atrophy of old age,—*senile atrophy*. As life advances, the vitality of the elements gradually diminishes, their ability to separate nutritive material from the blood and to assimilate it for their own maintenance becomes less and less, and hence they gradually atrophy, and ultimately all manifestations of their vitality may cease.

Although general atrophy may thus be referred to one of the foregoing causes, it is rarely a simple process, but usually depends upon the combined influence of two or more of them. The atrophy associated with pulmonary phthisis, for example, results partly from the loss of nutritive material in the profuse expectoration and diarrhoea, partly from the deficient supply consequent upon the imperfect oxidation of the blood and upon the interference with assimilation which is so often caused by structural changes in the stomach and intestines, and partly from the increased tissue-change. In senile atrophy, again, in addition to the general diminution of nutritive activity, there is frequently some condition of the digestive organs interfering with assimilation which materially aids in producing the ultimate result. The atrophy which accompanies the acute febrile diseases is by no means a simple process, increased tissue-change, loss of appetite, and interference with assimilation being all component parts of it.

Partial Atrophy may be caused by:—

1. *Imperfect Supply of Blood.*—The effect of interfering with the supply of blood to a part will depend upon the extent of the interference. If it be entirely cut off the part will die (see “Necrosis”), if merely diminished it will atrophy.

Diminished supply of arterial blood is a common cause of atrophy, and may be brought about in various ways. The nutrient vessels may be obstructed by pressure exercised upon them within or without the organ to which they are distributed. In cirrhosis of the liver, the pressure exercised by the new growth of inter-lobular tissue causes atrophy of the secreting structures. In other cases the supply of blood is diminished by interference with the circulation at some distance from the part, as by the pressure of a tumor upon the artery leading to it. The atrophy of the proximal end of the shaft of a bone after fracture above the point of entrance of its nutrient artery is due to the same cause.

The atrophies which result from pressure exercised directly upon the part itself are also owing to the consequent interference with nutritive supply. Atrophy of the sternum from the pressure of an aneurism, atrophy of the kidney from the pressure of retained secretion—as in stricture of the urethra, enlarged prostate, etc., and atrophy of the skull in chronic hydrocephalus, are well-known examples of these atrophies from pressure.

Mechanical congestion in the same way often leads to atrophy. The circulation is impeded, the blood is not returned normally by the

veins, hence there is deficient arterial supply, and atrophy results. This is seen, for example, in the liver of heart disease. (See "Mechanical Hyperæmia of Liver.")

2. *Diminished Functional Activity*.—This is the most common cause of atrophy, many examples of which are furnished both by physiological and pathological processes. After birth those parts which are no longer required to serve any purpose in the economy gradually atrophy and waste. The ductus arteriosus, the umbilical arteries and vein, the Wolffian bodies, and later—the thymus gland, all in this manner disappear. The involution of the uterus after delivery, the wasting of the spleen and lymphatic glands in advanced life, and of the lower jaw after the loss of the teeth, are other physiological examples of atrophy from this cause.

Muscles which from any cause have long remained inactive atrophy. This is seen in the various forms of paralysis; also in limbs which have become incapacitated, either on account of ankylosis, or of chronic disease of the bones or joints.

After the establishment of an artificial anus the lower part of the intestine atrophies, and becomes converted into a fibro-cellular cord.

Bones in the same manner atrophy from want of use. After the amputation of a limb the cut end of the bone atrophies; and atrophy of the orbit follows extirpation of the eyeball.

Interference with the function of nerves is also followed by their atrophy. This is seen in the atrophy of the optic nerve which often follows destruction of the eye, and also in the atrophy of the nerves of a limb which has long been incapable of action.

3. *Increased Functional Activity*.—This may in quite exceptional cases be a cause of atrophy; much more commonly, however, it is a cause of hypertrophy. Certain glands sometimes atrophy from excessive use, especially the testicle.

4. *The Action of Special Substances*.—Certain substances administered internally appear to be capable of producing atrophy. Iodine, bromine, mercury, lead, and the alkalies, may be enumerated amongst the most important of these. Iodine and mercury exercise a special influence upon the lymphatic system, and bromine upon the organs of generation.

5. *Nervous Influence*.—Respecting the influence of the nervous system as a *direct* cause of atrophy little is certainly known. That atrophy is a frequent sequence of changes in the nerve trunks and nervous centres there can be no doubt; but it is probably in most

cases to be attributed to an *indirect* influence. The gradual atrophy of muscles, for example, which have become paralyzed from lesions in the brain or spinal cord, is usually rather the result of the consequent interference with their function, than of any direct influence upon their nutrition. In lesions of certain portions of the nervous system, however, especially in those involving the large ganglion cells of the anterior cornua of the spinal cord, such as occur, for example, in infantile spinal paralysis, and also after some injuries of the nerve trunks, the muscles waste with great rapidity. In these and similar cases it must be assumed that the nutrition of the muscles is more or less *directly* influenced by the nervous system. (See "Introduction.") In some cases also, changes in the nervous system may cause atrophy by affecting the size of the bloodvessels, and so interfering with the supply of blood.

6. *Inflammation*.—This is sometimes described as a common cause of atrophy. The atrophy, however, which is such a frequent sequence of an inflammatory process is in most cases due to that new growth of fibroid tissue which is developed in chronic inflammations. The new tissue, by the pressure which it exercises, causes atrophy of the proper structures of the organ. This is seen, for example, in cirrhosis of the liver. It is probable, also, that the impairment of vitality which results from an inflammatory process may lead to atrophy of the histological elements, independently of the existence of new fibroid growth.

PHYSICAL CHARACTERS.—The estimation of atrophy is often a matter of considerable difficulty. The great criterion is diminution in absolute weight. The weight of an organ, however, varies considerably in health; it varies with the weight of the body as a whole, and it may be less than natural from incomplete development. The same is true also of the muscular and osseous systems. An accumulation of blood and serosity in an organ may again increase its weight, and thus constitute a source of fallacy. This is often the case in organs which have been for some time mechanically congested, in which, although their size and weight may be increased, their tissue is considerably diminished in amount.

Organs which are atrophied are usually diminished not only in weight, but also in size. In most cases they contain less blood, they are drier, firmer, and more fibrous in consistence than in health. Their functional powers are invariably diminished. The whole of the textures of which an organ is composed may suffer; some, however, usually do so more than others. The fibrous constituents are

the last to atrophy; hence the firmness, toughness, and loss of elasticity so commonly met with in the atrophied parts. In glandular organs, the secreting cells are usually the first to show signs of atrophy; they become smaller, and are often finely granular, from the presence of molecular fat; the vessels and nerves also share in the wasting process. In the subcutaneous cellular tissue, the fat is gradually removed from the cells, which thus diminish in size. In muscles the primitive fasciculi become smaller, and their transverse striæ gradually disappear; ultimately the whole of the contents of the sarcolemma may be entirely removed, and nothing remain but the connective tissue. This process is usually accompanied by more or less fatty degeneration of the muscular fibres, and in some cases by the development of fat between the fasciculi. (See "Fatty Infiltration of Muscle.")

Atrophy of Bone.

Atrophy of bone is always attended by a diminution in weight, but not always by a diminution in size. It is met with in two forms. In one, the compact and cancellous tissue gradually become absorbed, the medullary canal diminishes in size, and the whole bone thus becomes smaller. This is known as *concentric atrophy*. It is met with especially in the long bones, in cases of long-standing ankylosis, dislocations, or paralysis.

In the other variety of atrophy there is no diminution in the size of the bone, but merely a gradual conversion of compact into cancellous tissue. The whole bone thus becomes rarefied, and it is exceedingly light and brittle, so that it fractures with great facility. This, in contra-distinction to the former variety, is known as *eccentric atrophy*. It is usually met with as a senile change, and is in most cases accompanied by more or less fatty degeneration.

Pulmonary Vesicular Emphysema.

This appears to be the proper place to describe the changes met with in the lungs in emphysema, inasmuch as these changes are characterized mainly by atrophy of the walls of the air-vesicles.

Emphysema consists essentially in a permanent enlargement of the infundibula and air-vesicles in larger or smaller areas of the lungs. The dilatation appears usually to commence in the infundibulum, and

to extend from this to the air-vesicles which open into it, so that ultimately the whole may be thrown into one large cavity. As the process proceeds, communications are established between adjacent groups of air-vesicles, and thus cavities of still larger area are produced.

Atrophous Emphysema.—The more minute histological changes which accompany emphysema vary somewhat in different varieties of the disease. In that form of emphysema which occurs in old people, and which is essentially a senile change, the alterations in the walls of the air-vesicles consist simply of atrophy of the several structures of which they are composed:—hence the term *atrophous* or *small-lunged* emphysema, which is applied by Sir W. Jenner to this variety of the disease. The air-vesicles may not be much increased in size, but several of them are thrown into one, their walls are considerably thinner than natural, the connective tissue, elastic tissue, and blood-vessels all having apparently shared in the wasting process. There is usually also an abnormal amount of pigmentation. Such lungs are smaller than natural, and quickly collapse when the thorax is opened.

Hypertrophous Emphysema.—In the other important variety of emphysema the lungs are increased in size, so that they often bulge forwards when the thorax is opened, and in contradistinction to the former variety, certain constituents of the lung-tissue appear to be increased in amount, inasmuch as the lungs are less crepitant, and feel somewhat denser and tougher than natural. This is described by Sir W. Jenner as *hypertrophous* or *large-lunged* emphysema.

When such lungs are examined microscopically, it will be found that the dilatation of the air-vesicles is more marked than in atrophous emphysema, although less general in its distribution. The atrophic changes also do not affect equally the various tissues which make up the alveolar walls. The elastic fibres appear to be more especially wasted, whilst, according to some observers, the connective tissue is increased. I have been unable to discover any marked increase of the connective tissue in the alveolar walls, although an increase of this tissue is often to be seen around the smaller interlobular bloodvessels and bronchi. The capillary bloodvessels which are distributed on the walls of the air-vesicles are atrophied and diminished in calibre, owing to the stretching and pressure which result from the vesicular dilatation, whilst the larger interlobular vessels are often found thickened and distended with blood. In some cases there is

more or less fatty degeneration of the epithelium, and usually an abnormal pigmentation of the lung.

Etiology.—It would be beyond the scope of the present work to discuss the various theories which have been propounded to account for the development of emphysema. It is, however, obvious that all conditions which increase the pressure on the inside of the air-vesicles, or damage the resisting powers of their walls, may be causes of permanent vesicular dilatation.

Increased pressure on the inside of the air-vesicles may result from—

1st. Violent expiratory efforts with closed glottis, such as occur during the act of coughing, blowing wind instruments, violent muscular exertion, etc. Those parts of the lungs which are least supported will be over-distended. This is the expiratory theory of Jenner.

2d. Certain portions of the lungs being incapable of expansion, owing to collapse, consolidation, asthmatic spasm, etc. There will be excessive tension in those parts into which the air can enter.

Impairment of the resisting power of the air-vesicles may result from—

1st. The loss of elasticity and atrophy which is a concomitant of old age. This is the most important element in the causation of atrophous emphysema.

2d. The atrophy of the air-vesicles resulting from that stretching of their walls and obliteration of their bloodvessels which is caused by their over-distension from increased pressure exercised upon their inner surface.

3d. Damage to the walls of the air-vesicles which probably in certain cases results from previous attacks of pulmonary inflammation, or from some interference with their nutrition due to mode of life or to other causes.

Degeneration.

The “Degenerations” include a class of morbid processes which are characterized by an alteration in the *quality* of the tissues, and which, like atrophy, are attended by impairment of function, and often by annihilation of histological elements.

The alteration in the quality of the tissue results either from its direct metamorphosis into a new material, or from its infiltration with some substance which has been conveyed to it from without.

Atrophy and degeneration thus so far resemble one another, that in both processes nutrition is impaired and function interfered with. In atrophy, however, as pointed out by Virchow, nutrition is simply altered in *quantity*, the waste of the tissue is in excess of the assimilation of new material, and, consequently, there is a diminution in the amount of the tissue and an impairment of its functional powers. In degeneration, on the other hand, nutrition is altered in *quality*, a new substance exists in the tissues, which either originates in the tissue itself, or infiltrates it from without; this is attended by impairment of the vitality and functions of the elements of which the tissue is composed, resulting either from the presence of the new material, or dependent upon the same conditions as those which gave rise to its formation.

ETIOLOGY.—Of the causes of the Degenerations as a class, but little can be said, the various forms depending for the most part upon different conditions. These will be considered under their respective heads. Our knowledge of this class of morbid processes is necessarily very incomplete, inasmuch as so little is known of the chemical changes which take place within cells. (See “Physiology of Cells.”)

The Degenerations may be divided into two classes—the *Metamorphoses* and the *Infiltrations*.

1. *The Metamorphoses*.—These are characterized by the direct metamorphosis of the albuminoid constituents of the tissues into a new material. This is usually followed by the destruction of the histological elements and the softening of the intercellular substance, so that ultimately all trace of structure may be lost, and the function be completely arrested. The Metamorphoses include Fatty, Mucoid, Colloid, and probably Lardaceous Degeneration.

2. *The Infiltrations*.—These differ from the Metamorphoses inasmuch as the new material which exists in the tissues is not derived from their albuminoid constituents, but is deposited in them from the blood: there is an infiltration and deposition of a new substance. This is rarely followed by destruction of the histological elements, or by softening of the intercellular substance; hence the structure of the tissue is much less altered than in the Metamorphoses, and function is usually much less interfered with. The Infiltrations include Fatty, Calcareous, and Pigmentary Infiltration.

CHAPTER IV.

FATTY DEGENERATION.

FATTY Degeneration is an abnormal accumulation of fat in the tissues. An accumulation of fat occurs, however, under very different circumstances, and under the general term of "fatty degeneration" are included different pathological processes. Before proceeding to describe these processes and the histological changes which they produce, it will be well to consider, in the first place, the sources from which the fat met with in the body is derived; and secondly, the circumstances under which it may accumulate so as to constitute a morbid process.

General Pathology of Fatty Degeneration.—The chief source of the fat met with in the body is the oleaginous constituents of the food. A portion of these are stored up in the cells of certain tissues, to be utilized as producers of force and heat when the requirements of the system may demand it. The cells of adipose tissue, those of the medulla of bone, and, to a less extent, those of the liver, thus serve as physiological reservoirs for fat.

The other source from which fat may be derived is from saccharine and albuminous principles. The albuminous principles in the process of nutrition undergo decomposition, and the products of their decomposition contain a certain amount of fat. This is usually completely removed by oxidation, but under certain circumstances the oxidation is incomplete, and the fat accumulates in the cells of the tissue.

In considering the circumstances under which an accumulation of fat in the tissues may constitute a morbid process, it is to be remarked that it often becomes exceedingly difficult here to draw any sharp line of demarcation between health and disease. This is especially the case when the accumulation of fat is excessive in situations where fat is normally met with. When it occurs in abnormal situations the morbid nature of the process is evident.

An accumulation of fat in the tissues may occur so as to constitute a morbid process under the four following conditions:—

1st. When the food contains an excess of fat, or of substances capable of becoming converted into fat. Under such circumstances the oxygen taken into the body is insufficient to oxidize the excess, and it consequently accumulates in the cells.

An accumulation of fat from this cause occurs as a physiological process in the growth of adipose tissue. Adipose tissue is a connective tissue containing numerous cells which are distended with fat. The growth of this tissue thus consists simply in the fatty infiltration of more of these cells. (Fig. 5.) If this be excessive it constitutes

FIG. 5.



Fatty Infiltration of Connective Tissue. Showing the accumulation of fat within the cells.
 X 300. (Rindfleisch.)

obesity. The temporary accumulation of fat in the liver during the digestion of an aliment rich in fatty substances is another example of this kind of deposition. This will be described when speaking of the "fatty liver." If the amount of fat be very great it may accumulate, not only in normal situations, but also in tissues where fat is not usually met with, and in both cases the accumulation will thus constitute a morbid process.

2d. When there is no such excess of fatty substances in the food, but the processes of oxidation are so imperfectly performed, either locally or generally, that the fat contained in a natural diet is incompletely oxidized.

3d. When the fat which is liberated from the nitrogenous constituents of the food during the process of nutrition does not undergo the complete oxidation which it should, and so remains within the cells.

4th. When the fat which is liberated from the protoplasm of cells during the progress of nutrition is incompletely oxidized, and so accu-

mulates in, and takes the place of; the protoplasm. Here there is a gradual replacement of the protoplasm by molecular fat, so that the cell ultimately may be completely destroyed.

Fatty degeneration in which there is this destruction of histological elements is one of the most common forms of the disease, and it will hereafter be more fully described as *fatty metamorphosis*. Its nature was first pointed out by Dr. Quain in his well-known researches on fatty degeneration of the heart.¹ Dr. Quain then stated that the fat met with in the muscular fibres in this condition was the result of a metamorphosis of the fibres themselves, and was not derived from without. The truth of Dr. Quain's teaching has since been confirmed by the experimental investigations of Drs. Voit and Bauer.

Voit and Bauer's investigations were made with the object of determining the source of the fat in that acute form of fatty degeneration which is produced by poisoning with phosphorus, in which the degeneration is due mainly to the destruction of the red blood cells, and the consequent diminution in the oxidizing power of the blood.² They gave phosphorus to dogs which had for some days previously been starved, so that any fat which might be present in the tissues after death could not have been derived either from the food or from the adipose tissue of the animals. The phosphorus produced very extensive and general fatty degeneration, and the fat must obviously have arisen from the protoplasm of the cells. Voit concludes from these investigations—1st. That the transformation of albumin which takes place in cells is independent of the supply of oxygen, but that if the oxygen be deficient, the fat and other products of the transformation, being incompletely oxidized, accumulate in the cell. 2d. That the presence of fat in the cells may thus be due to increased transformation of the albumin, or to diminished oxidation of the products of its decomposition. 3d. That the fatty degeneration in poisoning by phosphorus is due both to an increased transformation of the albumin of the cells, and to diminished oxidation of the fat and other products of the transformation.

It will thus be seen that of the four conditions enumerated as causes of fatty degeneration, in all, with the exception of the first, the accumulation of the fat is principally due to incomplete oxidation, whilst in the first there is no imperfection in the oxidizing processes,

¹ "Medico-Chirurgical Trans. Lond.," 1850, vol. xxxiii.

² Voit and Bauer, "Zeitschrift für Biologie," vii. pp. 63-85; and Voit, "Neues Repertorium für Pharmacie," xx. pp. 340-349.

but the oxidizable materials are in excess. These two conditions are frequently associated.

Incompleteness of oxidation, and a consequent tendency to the production of fat, occurs under various circumstances. The red blood cells being the carriers of oxygen, all those conditions in which the supply of blood is interfered with, the red blood cells diminished in number or defective in quality, or the oxygenation of the blood imperfectly performed, may lead to fatty degeneration.

Interference with the supply of blood to a part and consequent fatty degeneration from imperfect oxidation may result from narrowing of the nutrient bloodvessels. This is seen in the heart as the result of atheromatous changes in the coronary arteries, and in organs in which the lumen of the vessels is diminished by lardaceous changes. The interference with the supply of blood caused by inflammation and mechanical congestion in the same way leads to fatty degeneration. Organs and tissues which have been long disused, and in which consequently the quantity of blood circulating through them and the oxidation processes become diminished, undergo fatty changes (see "Fatty Infiltration of Muscle"); as do also the cancers and other rapidly-growing tumors in which the rapidity of growth is out of proportion to the vascular supply.

An alteration in the blood as a whole, and a consequent general tendency to fatty changes, is seen in chlorosis and in those conditions of anæmia which are sometimes produced by chronic and acute diseases; also in the fatty degeneration which results from the destruction of the red blood cells by phosphorus. The long continued abuse of alcohol, and the influence of a high temperature, by diminishing the absorption of oxygen by the tissues tend to produce fatty changes. The senile forms of fatty degeneration, which affect especially the cornea and cartilage, are due to that diminution in the activity of the circulation which exists in old age. Lastly, the imperfect oxygenation of the blood which results from chronic diseases of the lungs constitutes an important element in the causation of the fatty degeneration which so frequently exists in these diseases.

In proceeding to consider the histological changes which are produced in the tissues by an accumulation of fat, it is in the first place to be remarked that in those cases in which the fat is derived from the food, it is, for the most part, deposited in those situations in which fat is normally met with; whereas when it originates in the tissues it may occur in the cells of any part. The changes produced in the tissues

must obviously vary in the two cases. Where the fat is derived from the metamorphosis of the nitrogenous constituents of cells, the process is accompanied by more or less destruction of the cell, and by a corresponding impairment of its functional powers—the tissues are destroyed in the process; whilst in the other cases no such destruction usually takes place. Although these two conditions may occasionally be associated, yet, owing to the marked difference in the results which they respectively produce, it will be well to speak of them separately; that in which the fat is derived from the metamorphosis of the tissues being termed *Fatty Metamorphosis*, that in which it is derived from the oleaginous, saccharine, or nitrogenous principles of the food *Fatty Infiltration*.

Fatty Infiltration.

In Fatty Infiltration, the fat which is deposited within the cells usually occurs as distinct drops of oil. In the earliest stages of the process these are very small, but as the deposition proceeds they gradually accumulate and run together, displacing and obscuring the nucleus and protoplasm, until the cell is completely filled and distended with oil. (Fig. 6.) The vitality and functions of the cells are but little impaired by the accumulation, and the protoplasm—although rendered almost invisible when this is excessive—remains unaltered. The cells within which the fat accumulates not being destroyed, the removal of the fat is all that is necessary to restore them to their original condition. As already stated, fatty infiltration occurs as a physiological process in the growth of adipose tissue, and also in the liver during the digestion of an aliment rich in fatty substances.



FIG. 6.
Liver Cells in various stages of Fatty Infiltration. × 300. (Rindfleisch.)

Fatty Infiltration of Muscle.

In muscle, fatty infiltration is frequently met with as a morbid process. The cells in the connective tissue which surrounds the fasciculi of the muscle become filled with fat; and this development of fat between the primitive muscular fasciculi has often been confounded with degeneration of the fibres themselves. In this latter process, however, which will subsequently be described as *fatty metamorphosis*

of muscle, there is a direct metamorphosis of the muscular fibres into fat; whereas in the condition now under consideration, there is a deposition of fat *between* the fasciculi, which remain—during the early stages, at all events—unaffected. The interstitial fat varies in amount. In some cases single rows of fat cells alternate with rows of muscular fasciculi; at other times the accumulation is less regular, more existing between some fibres than between others: in all cases, however, the muscular elements may be discovered lying amongst the fat. (Fig. 7.) If the latter be very considerable in amount, the

FIG. 7.



Fatty Infiltration of Heart. A section from the more external portion of the left ventricle of the heart, showing the growth of fat *between* the muscular fibres. The fibres are in some places atrophied and commencing to undergo fatty metamorphosis. $\times 200$.

muscle may appear to the naked eye to be entirely converted into fat; but the microscope will always reveal the muscular structure in which it is embedded.

This condition is frequently met with in animals which have been fattened, the fat increasing not only in the usual situations, but also accumulating between the fasciculi of the muscles. In muscles also which from any cause have for some time been incapacitated, and in which consequently the circulation of blood and the oxidation processes are reduced to a minimum, this interstitial growth is extremely

liable to occur—*ex. gr.*, in the extensors of the wrist-joint in cases of lead-poisoning, and in long standing paralyses from lesions of the brain or cord, also in muscles which have been rendered useless by ankylosis of a joint. In progressive muscular atrophy, as Virchow has shown, the affected muscles exhibit this change, together with true fatty metamorphosis.

Fatty Infiltration of the Heart.—In the heart fatty infiltration is not unfrequently met with; and here it is especially important to distinguish it from the much more grave condition in which the fibres themselves are primarily affected. In health, there is a varying amount of fat covering the surface of the heart beneath the visceral layer of the pericardium, which is always most abundant in the grooves between the auricles and ventricles, where it surrounds the bloodvessels. This may increase so as to completely envelop the organ, and at the same time gradually insinuate itself between the muscular fibres, so that to the naked eye all appearance of muscular structure may be lost, the walls looking like a mass of fat. In hearts less affected, striæ of fat will be seen lying amongst the muscle. (See Fig. 7.) The fat is always most abundant near the surface, the muscular structure becoming more evident towards the endocardium.

The immediate effect of the interstitial growth is to displace and compress the muscular fibres between which it insinuates itself, and in doing so it diminishes the contractile power of the muscle. This is especially important when occurring in the heart. The pressure, however, which it exercises upon the fibres and the accompanying bloodvessels, ultimately causes atrophic and degenerative changes. Thus the fasciculi gradually atrophy, the transverse striation becomes indistinct and is replaced by molecular fat; in fine, true metamorphosis of the muscle is established. These two processes, indeed, not uncommonly go hand in hand together, the interstitial infiltration preceding the intrastitial metamorphosis.

Fatty Infiltration of the Liver.

In the liver fatty infiltration is exceedingly frequent, constituting what is commonly known as the “fatty liver.” The hepatic cells always contain a small quantity of fat, which is temporarily increased after the ingestion of fatty substances. It will be well to describe this physiological infiltration before proceeding to the morbid process.

The ingestion of an aliment rich in fatty substances is followed by

a temporary excess of fat in the portal blood, and by the deposition and temporary accumulation of a portion of this within the hepatic cells. This fat is first deposited in the cells which are in immediate contact with the capillaries of the portal vein, and thus is produced an excess of fat in the cells at the circumference of the hepatic lobules. This gradually passes from the cells at the circumference to those in the interior, whence it is ultimately conveyed again into the circulation. This process goes on until the excess of fat is removed from the blood, when the hepatic cells again acquire their former character. There is thus a transitory accumulation of fat within the hepatic cells which is gradually removed, the vitality of the cells not being thereby impaired.

The morbidly fatty liver is one which contains an abnormal quantity of fat, and here also, as the fat is usually deposited from the blood in the portal capillaries, the increase is first observable in the external zone of the hepatic lobules. (Fig. 18.) It accumulates here within



Fatty Liver. Showing the accumulation of fat in those cells more especially which are situated in the external zone of the lobule. There is also an increase in the interlobular connective tissue (Cirrhosis). V. Hepatic vein. I. Interlobular connective tissue. $\times 50$.

the cells as minute globules, which as they increase coalesce and form large drops of fat. These ultimately completely fill and distend the cells which at the same time become larger and more globular in

shape. (See Fig. 6.) As the process proceeds, the accumulation advances from the periphery towards the centre of the lobule, until its whole mass may be involved, and the cells universally become distended with fat. The vitality of the cells is not materially impaired by the infiltration; they continue to perform their functions, as is shown by the presence of bile in the stools and in the gall-bladder. In some exceptional cases the accumulation of fat is most marked around the hepatic vein. This, according to Virchow, is probably to be explained by supposing that the fat is becoming excreted, and that only the last cells retain a little of it.

The fatty liver is somewhat increased in size, in advanced stages often considerably so. The surface is smooth, the edges are thickened and rounded, the specific gravity is diminished, although the absolute weight may be increased. If the infiltration be slight, involving merely the portal zone of the lobules, the cut surface will present a mottled appearance, the external fatty zone being of an opaque yellowish-white color, whilst the central portion remains unaltered, or is perhaps somewhat hyperæmic. The more extensive the infiltration the larger is the pale zone, and ultimately, when the whole lobule is involved, there may be left in the centre merely a reddish-brown point, which corresponds with the commencement of the hepatic vein; and in many cases even this point is lost. The organ is then of an almost uniform opaque yellowish-white color, and the boundary between the individual lobules may be completely obscured. In exceptional cases the accumulation of fat is much more abundant in some portions of the liver than in others, so that on section, yellowish points and streaks are seen scattered over its surface. The consistence of the organ is much diminished, it feels doughy, and pits on pressure with the finger, and the knife used to cut it becomes coated with oil. The pressure exercised by the infiltrated fat produces considerable anæmia of the organ, but the interference with the circulation is never sufficient to cause ascites, hemorrhage, or other evidences of portal congestion.

The liver is especially liable to become the seat of fatty accumulation. This, as shown by the late Dr. Bence Jones, is owing—firstly, to the excess of non-nitrogenous oxidizable matter in the portal blood; secondly to the deoxidized condition of the portal blood; and thirdly, to the low pressure and slowness of circulation in the portal vessels—conditions the least favorable to oxidation.¹

¹ "Lectures on Pathology and Therapeutics." Dr. Bence Jones, p. 179.

An accumulation of fat in the liver occurs under two opposite conditions—one in which there is general obesity, and the fat accumulates in the liver in common with other parts; and another, in which there is general emaciation, and a consequent impairment of the oxygenating power of the blood. The fatty infiltration of the liver which is so constantly associated with certain chronic diseases of the lungs, is also partly due to imperfect oxygenation of the blood from destruction of lung-tissue. Fatty liver caused by phosphorus and other poisons has been already alluded to.

The other variety of fatty degeneration—fatty metamorphosis—will be described in the following chapter.

CHAPTER V.

FATTY DEGENERATION (*continued*).

Fatty Metamorphosis.

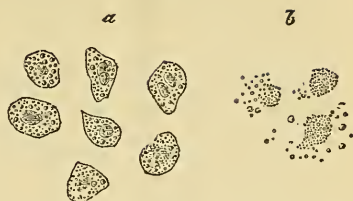
THIS differs from fatty infiltration, inasmuch as the fat is derived from the albuminous constituents of the tissues themselves, and not from the fatty, saccharine, or nitrogenous principles of the food.

The process consists in the gradual replacement of the protoplasm of cells by molecular fat, in the manner described in the preceding chapter. The fat makes its appearance as minute granules and molecules, usually first in the protoplasm, and subsequently in the nucleus. The granules—which are characterized by their dark color, sharp contour, strong refractive power, and solubility in ether—gradually increase in number, and ultimately the whole of the protoplasm may be transformed. As they increase some of them may coalesce, and so form distinct drops of fat. As the process proceeds the cells undergo an increase in size and become more globular in shape, the nucleus becomes involved, the cell-wall, when this exists, is destroyed, and the cell may thus be converted into a mass of granular fat. (Fig. 9.)

These granules of fat sometimes remain for some time in a coherent form, and they then constitute what were formerly known as the

"inflammatory" or "exudation corpuscles," or "corpuscles of Gluge," which are so common in chronic cerebral softening, and in some other forms of fatty degeneration. (Fig. 9, *b*.) Ultimately the albuminous matter between the granules of fat liquefies, the corpuscles break up, and the fat becomes distributed in the tissue (Fig. 9, *b*). These granular corpuscles will be more fully considered when speaking of cerebral softening.

FIG. 9.



Fatty Metamorphosis of Cells. *a.* From a cancer. *b.* From the brain in chronic softening. The latter show the large "granular corpuscles," and also the manner in which these become disintegrated. $\times 200$.

Types of this pathological process are furnished by many well-known physiological ones, one of the most characteristic of which is perhaps the secretion of milk. The secretion of milk takes place in the following manner: The mammary gland becomes exceedingly vascular, white blood-corpuscles escape from the vessels, the epithelium multiplies, and a large number of young cells thus make their appearance in the ducts of the gland. These cells as they are produced become converted into fat, the cells break up, and the fatty matters in a more or less coherent form constitute the milk-corpuscles. In the earliest stages of the process the granules of fat cohere and form the colostrum-corpuscles, which are precisely analogous to the large granular corpuscles met with in chronic cerebral softening, etc. (Fig. 9, *b*); but as the secretion becomes fully established, and the disintegration of the cells takes place more rapidly, the fatty molecules become at once distributed in the liquid in which they are suspended, giving to the secretion its characteristic white color. The milk-corpuscles thus formed are replaced continuously by new cells, which in their turn undergo fatty metamorphosis, and in this manner a continuous formation and destruction of cells take place. Other examples of fatty metamorphosis are afforded by the formation of the sebaceous matter of the skin, the cerumen of the ears, and the corpus luteum in the ovary; all of which take place in the same way by the fatty metamorphosis and destruction of newly formed cells.

The immediate effect of fatty metamorphosis is to produce more or less softening of the affected part, and necessarily to impair or annihilate function. If large tracts of tissue are affected, the change is readily recognizable by the diminution in consistence and elasticity which are produced, and in many cases also by the opaque yellowish-

white color. If, however, the change is limited to minute portions of the tissues, its existence can only be discovered with the aid of the microscope.

The fatty particles into which the cells have been transformed are, under favorable circumstances, readily absorbed. The fat may thus be removed and the degenerative process cease before the part has been dangerously involved. Such recovery probably often occurs, for example, in the kidneys and heart. When the elements are completely degenerated the fatty débris is also usually removed by absorption. This is seen in the fatty degeneration and absorption of inflammatory products, such as occurs in croupous pneumonia. In order for such absorption to take place it is necessary that the tissue should be freely supplied with bloodvessels. If this is not the case, the degenerated products are liable to undergo certain changes whereby they become converted into a pultaceous crumbling material somewhat resembling cheese:—this is known as *caseation*.

CASEATION.—This is a modification of the degenerative process in which the fatty products gradually dry up into a yellowish friable material, which has been compared to soft cheese. This change appears to be owing to a natural dryness of the degenerated tissue, resulting from deficient vascular supply. It is most frequent in parts which contain but few vessels, or in those in which these become obliterated by inflammatory products or by some new growth. Growths composed of closely-crowded-cells—as epithelial accumulations within the pulmonary alveoli, growths in the lymphatic glands, in the brain, and in osseous structures, are the most liable to become caseous.

The process consists in a gradual drying up of the degenerated elements; the fluids are absorbed, the cells—which are many of them incompletely degenerated—shrivel and atrophy, the fat undergoes partial saponification, cholesterine forms, and the tissue thus becomes converted into a soft, yellowish-white, cheesy substance, composed of atrophied cells, fatty débris, and cholesterine crystals. This material may gradually dry up more and more, and ultimately become encapsuled by a layer of fibrous tissue.

These cheesy matters are constantly met with, especially in the lungs, and considerable confusion has arisen as to their nature and origin in this situation. This has proceeded from its having been formerly the custom to look upon all cheesy masses as essentially tubercular. Tubercle, it is true, often undergoes, to a greater or less

extent, fatty degeneration, and it may thus, like all other growths which have undergone this process, become converted into a yellow cheesy substance ; but it is by no means true that all cheesy masses are tubercular. The pathological significance of caseation is thus less limited than was formerly supposed, and although this change is undoubtedly most common in tuberculous and scrofulous lesions, its occurrence merely indicates that the elements have undergone fatty metamorphosis, and under no circumstances is it in itself evidence of any one particular form of morbid growth. (See "Scrofulous Inflammation.")

The caseous mass may subsequently become calcified, or undergo a process of softening and liquefaction.

CALCIFICATION.—This is an advanced stage of the preceding process. It most frequently occurs in those cases in which the caseous mass is completely inclosed and isolated from the external air, as when in the lymphatic glands, in bone, or when encapsuled in the lungs. The mass becomes infiltrated with calcareous particles, and is thus converted into a calcareous concretion. (See "Calcareous Degeneration.")

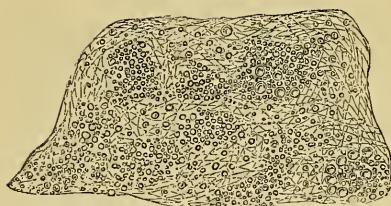
SOFTENING.—This process consists in a liquefaction of caseous substance, which is probably owing to some chemical change in its constituents. It most commonly occurs in parts which come into contact with the external air, especially in those situated in the lungs. The caseous mass liquefies, and is converted into a thin puriform liquid, containing curd-like cheesy matter, which to the naked eye looks much like pus, but under the microscope is seen to consist simply of granular débris, fat, and cholesterine crystals. This, if not discharged, may, like the caseous masses, ultimately dry up and become calcified.

Fatty Degeneration of Arteries.

Fatty degeneration of arteries may be a primary or secondary affection. As a secondary process it is met with in atheroma and other inflammatory conditions of the vessels, in which the fatty change is preceded by a cellular infiltration of the sub-endothelial connective tissue. (See "Atheroma.")

Primary fatty degeneration is a passive process, not being preceded by any increased nutritive activity of the parts affected by it. It may affect both the internal, middle, and external coats of the artery, but it is most common in the first-named situation. The change usually

FIG. 10.



Fatty Degeneration of the Internal Coat of the Aorta. Small yellowish-white patches scattered over the lining membrane of the vessel. A very thin layer peeled off and $\times 200$, showing the groups of fat molecules, and the distribution of fat in the intima.

commences in the endothelium and the connective tissue cells in the most internal layers of the inner coat, small groups of cells becoming affected in various parts of the vessel; and it may gradually extend from within outwards, the intercellular substance softening, until, in exceptional cases, the whole thickness of the intima is destroyed. (Fig. 10.)

In the earlier stages of the process the condition is recognized by the existence of small, irregular-shaped patches of an opaque yellowish-white color, projecting very slightly above the surface of the intima. These, which are so constantly met with on the lining membrane of the aorta, may at first be mistaken for atheroma. They are in most cases, however, readily distinguishable by their superficiality, and by the facility with which they can be stripped off from the subjacent layers, which present a natural appearance. In atheroma, on the other hand—which affects the deeper structures—if the superficial layer be removed, the opacity and thickening are seen to exist beneath it. In many cases the change is limited entirely to the innermost layers of the vessel; the more the subjacent tissues are involved, the greater is the irregularity in the shape of the patches, and the less readily can they be separated with the forceps. The opaque patches occasionally break down, the cells are destroyed, the intercellular substance softens, and the granular debris is carried away by the circulation, leaving small, irregular, superficial erosions upon the lining membrane of the vessel. These erosions are not ulcers in the true sense of that term, not being the result of an active process. They resemble the superficial erosions so common upon the mucous membrane of the stomach, as described by Dr. Wilson Fox.

Simple fatty degeneration may occur in any of the arteries, but it is in the smaller ones that its injurious influence is most marked, and in these it is more especially liable to affect the external coat. (Fig. 11.) Here, by diminishing the elasticity and contractility of the vessels, it causes degenerative changes in the parts which they supply, and often leads to rupture. This is exemplified by many cases of chronic cerebral softening and cerebral hemorrhages, although

here atheromatous are often associated with the fatty changes. In the larger arteries, as the aorta—where it is exceedingly common—it is of less importance, the inflammatory process, atheroma, having here a far more deleterious effect.

Fatty Degeneration of Capillaries.—The capillaries may also be the seat of fatty changes. Here they are most common in the nervous centres, and in the kidneys in Bright's disease. (See Fig. 11, *b*.) The process commences in the endothelial cells, and may involve considerable areas of the capillary wall, so that rupture is often the ultimate result. This is common in the smallest cerebral bloodvessels, where it is sometimes a cause of cerebral (capillary) hemorrhage.

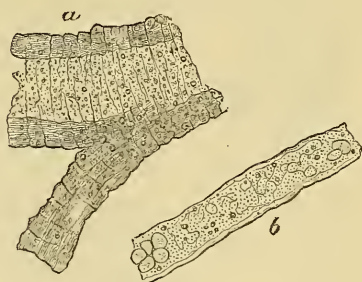
Primary fatty degeneration of bloodvessels is in most cases a senile change; it is an expression of that general impairment of vitality which exists in advanced life, and is usually associated with similar changes in other parts. When, however, it is limited to the lining membrane of the largest arteries it is often met with in early life and in persons who are otherwise perfectly healthy. Fatty degeneration secondary to inflammatory conditions will be considered subsequently. (See "Inflammation of Bloodvessels.")

Fatty Degeneration of Muscle.

Both striated and non-striated muscle may be the seat of fatty degeneration. In the latter, the muscular fibre-cells are the seat of the change; they become filled with fat granules and are ultimately destroyed. This condition is frequently met with in the middle coat of arteries which are undergoing fatty degeneration.

In striated muscle—both in the voluntary and in the involuntary of the heart—the fibres themselves are the seat of the morbid process, which consists in the replacement of the albuminous matter of which the fibre is composed by fat. The earliest stage of the affection is characterized by an indistinctness in the transverse markings of the fibres, which in many parts become studded with minute particles of

FIG. 11.



Fatty Degeneration of Small Vessels of Pia Mater. From a case of chronic Bright's Disease. *a*. A small artery, the coats of which are somewhat thickened. *b*. A capillary, in which are seen a few red blood-corpuscles. $\times 400$.

fat. (Fig. 12.) These gradually increase in number and size, and are usually distributed somewhat irregularly within the sarcolemma.

FIG. 12.



Fatty Degeneration of Muscular Fibres of Heart.
a. Earlier stage.
b. More advanced.
X 400.

In some parts single rows of granules are found running along the length of the fibre; in others, they are grouped around the nuclei or arranged in transverse lines corresponding with the striæ of the muscle. The fibres become extremely friable, and are readily broken up into short fragments. As the process proceeds the transverse markings entirely disappear, and nothing but molecular fat and oil-globules are seen within the sarcolemma. The sarcolemma itself may ultimately be destroyed, and nothing remain of the original fibre but the fatty

débris into which its albuminous constituents have been converted. This is true fatty degeneration of muscle; in it the muscular elements are destroyed, and it thus differs essentially from fatty *infiltration*, in which there is simply a development of fat between the fasciculi, the fasciculi themselves not being primarily affected. (See "Fatty Infiltration of Muscle.")

Fatty Degeneration of the Heart.

It is in the heart that fatty degeneration of muscle is most frequently met with, and here it assumes a most important aspect from the deleterious influence which it exercises upon the motor power of the organ. The muscular substance may be affected throughout, or the degeneration may be confined to certain portions of it. The wider the extent of tissue that is affected, the less advanced, as a rule, is the degree of the degeneration. It is in those cases in which small tracts of tissue only are involved that the process is met with in its most advanced stage.

When the change is slight and more or less general, the muscle is somewhat softer and more flabby than natural; it is more friable, and often breaks with a soft granular fracture; and its color is rather paler and more opaque than that of healthy cardiac tissue. Under the microscope the muscular fibres are seen to have lost to some extent their striated appearance, and to contain granules of fat. (Fig. 12, a.)

This diffuse form of degeneration may occur in the course of those diseases in which the oxidation processes are reduced to a mini-

mum; in all those diseases, in short, which are attended by marked anæmia, whether this anæmia be gradually or rapidly induced. In the case from which the accompanying drawing was taken, the degeneration was acute. (Fig. 13.) This was the case of a weakly young

FIG. 13.



Acute Fatty Degeneration of Heart and of other Muscles. a. Heart. b. Rectus abdominis. The whole of the heart-tissue was affected, and also the muscles in other parts of the body. $\times 400$.

girl who was under my care suffering from slight valvular disease. She quickly succumbed with acute fatty degeneration of the heart and other muscles, which was induced by a profuse loss of blood during a menstrual period, and by inability to retain food.¹ Interference with the circulation in the coronary arteries is also a frequent cause of a more or less general degeneration of the muscular tissue. This occurs especially as a result of aortic incompetence, and explains the early failure of cardiac power in this form of valvular disease. Atheromatous changes in these arteries, such as result from the increased blood-pressure of Bright's disease, lead in the same way to fatty degeneration. Lastly, in its slightest degrees, a diffuse fatty degeneration of the heart sometimes occurs in the course of acute febrile diseases. This will be again referred to in the chapter treating of the histological changes produced by pyrexia.

¹ This case is reported in "Trans. Clinical Society, London," vol. viii. 1875.

Sometimes the degeneration, although perhaps more or less general, is much more advanced in some parts than in others. In such cases the heart presents a mottled appearance; opaque pale yellowish or brownish patches are seen irregularly distributed throughout its substance. These patches, which vary considerably in size and form, are met with especially in the papillary muscles, the columnæ carneæ, and in the layers of fibres immediately beneath the endocardium. They may also occur beneath the pericardium, and in the deeper portions of the organ. They correspond with the most degenerated portions of the tissue. They are soft and flabby, and have a rotten consistence, tearing readily under the finger. Under the microscope, the fibres are seen to be in an advanced stage of fatty degeneration, their sarcolemma containing molecules of fat and oil globules, which in many parts have escaped and lie free amongst the surrounding less degenerated tissues. (Fig. 12, *b*.) These more localized degenerations are most common in old people, and usually result from considerable disease of some branches of the coronary bloodvessels, and not from conditions of general anæmia. The peripheral layers of muscular tissue also frequently undergo extensive fatty degeneration as the result of pericarditis. The connection between these localized degenerations and rupture and aneurism of the heart is well known.

BROWN ATROPHY OF THE HEART.—Somewhat allied to, and occasionally associated with, fatty degeneration of the heart, is the condition known as brown atrophy. This consists in a gradual atrophy of the muscular fibres, together with the formation of granules of brownish-yellow or blackish pigment. These granules of pigment, which are probably the coloring matter of the muscles, are either grouped in clusters around the nuclei, or more generally distributed within the fibre. The fibres are frequently, at the same time, the seat of more or less fatty degeneration. (Fig. 14.) This change usually occurs as a senile one, or as a part of general marasmus from other causes. It is also met with in some cases of cardiac hypertrophy. Its recognition is in most cases impossible without the aid of the microscope.

FIG. 14.



Brown Atrophy of the Heart. Showing the granules of pigment and the atrophy of the fibres. The latter have in some parts undergone slight fatty metamorphosis. $\times 400$.

Fatty Degeneration of the Kidneys.

Fatty degeneration of the kidneys frequently occurs as a result of inflammation of the organs. This *secondary* degeneration will be alluded to when treating of renal inflammations. Primary fatty degeneration is much less frequent. It must be borne in mind that the renal epithelium very commonly contains more or less fat; but it is only when this is excessive that it can be regarded as a diseased condition. This excessive formation of fat in the kidney is, I think, less common than is generally supposed. It is, however, occasionally met with in chronic diseases, especially in pulmonary phthisis. It is also a result of poisoning by phosphorus.

In simple fatty degeneration the change is usually confined to the epithelium of the cortex. The cortex presents on section a somewhat yellowish-white surface, often slightly mottled, and this, in most cases, is most marked near the bases of the pyramids. There is no adhesion of the capsule or granulation of the surface. This change appears to interfere but little, if any, with the functions of the organs, and in this respect it resembles the analogous change in the liver. It is not usually accompanied by albuminuria.

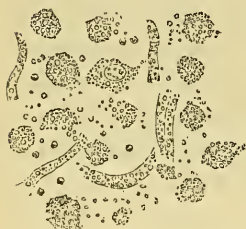
Cerebral Softening.

This is perhaps the most suitable place to speak of cerebral softening, inasmuch as fatty degeneration of the brain-tissue usually constitutes a prominent feature in the histological changes. Softening of the cerebral substance is essentially a necrotic process, and may result from all those conditions which interfere with vascular supply. The portions of the brain which are the seat of this change may be merely rather softer than the surrounding healthy tissue—breaking down more readily under a stream of water which is allowed to fall upon them—or they may be completely diffuent. They are never distinctly circumscribed, but pass by insensible gradations into the neighboring tissue.

Under the microscope the change is seen to consist in a disintegration of the nerve-tissue. The white substance of the fibres first coagulates, then breaks up into masses of various sizes (myeline), and these usually undergo more or less fatty metamorphosis. The cells of the neuroglia, the small bloodvessels, and, when the gray matter is implicated, the large nerve-cells, are also involved in the necrotic

change. The tissue is thus converted into broken-down fibres, granular matter, and molecular fat, and amongst this are numbers of the large granular corpuscles already alluded to (Fig. 15). These corpuscles, as previously stated, although formerly looked upon as the result of inflammation, appear to be simply conglomerations of granular matter resulting from the degeneration of cellular elements (see Fig. 9), and in the brain, where they are much the most common, many of the granules are probably myeline and not fat. These corpuscles are exceedingly characteristic of cerebral softening. They vary in size from $\frac{1}{500}$ to $\frac{1}{200}$ inch in diameter, and originate, according to Virchow and Robin, from the cells of the neuroglia—the connective tissue of

FIG. 15.



Chronic White Softening of the Brain. Showing the granular corpuscles, broken-down nerve-fibres, and fat granules, of which the softened substance is composed. One or two nucleated cells (probably nerve-cells) are also visible. $\times 250$.

the brain. The small arteries and capillaries running through the softened part are many of them filled with granules and granular cells, the latter probably originating in the white blood-corpuscles which have accumulated in the part and undergone fatty changes. As the process proceeds the cerebral substance is completely destroyed and all trace of nerve-structure is ultimately lost.¹

The color of the softened portion varies considerably. It may resemble that of the surrounding healthy tissue, or be of a yellowish or reddish tint. According to these variations in color, cerebral softenings have been classified into *white*, *yellow*, and *red*.

The color depends in great measure upon the amount of blood contained in the part, and on this account is important, as indicating the manner in which the softening has been brought about.

White Softening.—This is, in the great majority of cases, a chronic process. It occurs especially in old people, and is usually due to that disease of the smaller cerebral bloodvessels and consequent interference with the circulation which is common as a result of age. The impairment of the contractile power of the heart must also constitute an auxiliary in the causation of the imperfect vascular supply. It is the gradual manner in which the supply of blood is diminished

¹ According to Prof. Cohnheim the granular corpuscles are white blood-cells impregnated with fatty or other particles derived from the surrounding degenerated tissue.—*Vorlesungen ueber Allg. Pathologie*, Band 1.

which accounts for the absence of hyperæmia or hemorrhage, so that the color of the softened portion either resembles that of healthy brain-tissue, or is an opaque dirty white. White softening is sometimes acute, in which case it is usually due to the sudden obstruction of the circulation by the impaction of an embolus in one of the *larger* arteries. (See "Embolism of the Brain.")

Yellow Softening.—This is, in most cases, simply a variety of the former process, in which, from the fine state of division and close aggregation of the granular matter, a dead yellowish-white color is imparted to the softening tissue. This color is probably often partly owing to the presence of altered blood pigments, the result of some previous slight extravasation. The pigment may sometimes be seen as fine dark granules, scattered through the cells of the neuroglia and the nerve-cells of the gray matter, where at first sight they look like fatty particles: they are distinguished, however, by their dark black color. A softening of the brain more rapidly induced, as by embolism or thrombosis, may also occasionally be of a yellow color. This, however, is only the case when the softened portion has attained a certain age, and much of the extravasated blood has been removed by absorption. Lastly, a condition of gelatinous œdema of a yellow color, which has been described by Rokitsansky as often being present in the immediate vicinity of cerebral tumors, has been regarded as a variety of yellow softening.

Red Softening.—This is commonly a more acute affection, most frequently dependent upon vascular obstruction, either from embolism or thrombosis. There is collateral hyperæmia, rupture of capillaries, and extravasation of blood; the softened tissue is consequently of a deep red color. These forms of softening will be described in the chapter on "Embolism." Red softening is also sometimes associated with the chronic white variety, some of the diseased vessels giving way, and thus extravasation of blood taking place into the already softened tissue. Lastly, red softening may be inflammatory. (See "Inflammation of the Brain.")

CHAPTER VI.

MUCOID AND COLLOID DEGENERATION.

UNDER this head is included a class of morbid changes which are characterized by a peculiar softening of the tissues. Colloid and mucoid degeneration have frequently been described under the common term of "colloid softenings," but, although they are very closely allied and sometimes associated, they appear to constitute two distinct processes; the former affecting more especially the cells, the latter the intercellular substance.

MUCOID DEGENERATION.—This consists in the transformation of the albuminoid constituents of the tissues into *mucin*, owing to which they become converted into a material of a soft, mucilaginous, jelly-like consistence. This is the condition of nearly all tissues in their immature or foetal state; the connective tissues in the foetus consist almost entirely of this soft mucin-yielding substance. Some tissues retain these characters after birth. The umbilical cord, and the vitreous humor of the eye, are both composed of this substance.

A mucoid change occurs as a physiological process in the secretion of mucus. The newly-formed cells undergo mucoid transformation, which results in their destruction, and the mucus is thus liberated. It is considered probable by some that the cells may also evacuate the mucus without being destroyed. This process occurs much more rapidly in all catarrhal conditions of the mucous membrane.

As a pathological process mucoid degeneration affects especially the intercellular substance. The intercellular substance of the connective tissues in their fully developed state consists of gelatin and chondrin, and the mucoid change is thus a reversion of this substance to its foetal condition.

Mucin is closely allied to albumen, more so than to either gelatin or chondrin: it differs from it in not containing sulphur. Like albumen, it is only met with in alkaline fluids—being held in solution by the free alkali—from which it is precipitated by dilute acetic acid. It differs from albumen in being insoluble in an excess of the acid, and also in not being precipitated by boiling, by tannin, or by bi-

chloride of mercury. Its behavior with these two reagents will also distinguish it from gelatin and chondrin, which are both precipitated by them.

The mucoid change is by no means a common one. It is most frequently met with in cartilage, especially in the inter-vertebral and costal cartilages of old people. It also occurs in serous membranes, in bone, and in many of the new formations, especially in those of the connective tissue class. Wherever it occurs it produces softening of the affected parts; which are transformed into a homogeneous, colorless material, of a soft mucilaginous jelly-like consistence. If the change is limited to isolated portions of the tissue, the softened parts surrounded by those which are unaltered, often present the appearance of cysts. These cyst-like formations containing mucoid substance are not uncommonly met with in the costal cartilages and in new growths.

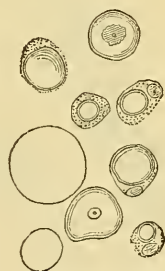
As to the cause of the mucoid change, nothing is known.

COLLOID DEGENERATION.—This differs from the former, inasmuch as it is the cells which are more especially involved in the process.

The change consists in the metamorphosis of the albuminoid constituents of the cells into a substance known as *colloid* material. Colloid closely resembles mucin, but it differs from it chemically, in containing sulphur, and in not being precipitated by acetic acid. It is a colorless, transparent, glistening material of the consistence of jelly or half-set glue. It makes its appearance within the cells as small lumps, which gradually increase in size, pushing the nucleus to one side, until they completely fill the cell. (Fig. 16.) The cells are thus destroyed, and converted into colloid masses. The small colloid masses subsequently swell up, coalesce, and so form larger masses of firm, transparent, yellowish, jelly-like material, which are readily to be recognized by the naked eye. As the colloid matter increases, and the cells are destroyed, the intercellular substance atrophies or softens, and in this way cyst-like cavities are formed, within which is contained the gelatinous substance. Here it may subsequently undergo a process of liquefaction. (See Fig. 58.)

The colloid change is most common in enlargements of the thyroid gland (goitre), in the lymphatic glands, in the choroid plexus, and in many of the new formations.

FIG. 16.



Colloid Cells, from
a colloid cancer.
(Rindfleisch.)

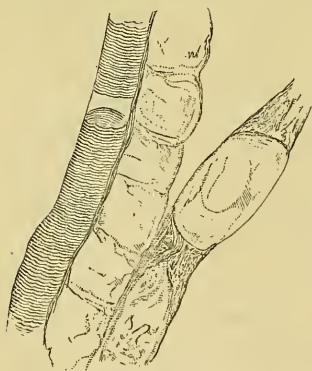
(See "Colloid Cancer.") Its causes and nature are as obscure as those of the allied mucoid softening.

It is when occurring in new formations that these two forms of degeneration assume their most important aspects. Certain varieties of tumors may originate as mucoid or colloid growths, or may subsequently undergo these morbid transformations. The mucous tumors (myxomata), which resemble in structure the umbilical cord, consist entirely of a gelatinous mucin-yielding substance. The sarcomata, lipomata, enchondromata, and the cancers may also become the seats of these forms of softening. Such growths have sometimes been described as gelatiniform or colloid *cancers*, this term having been applied to them without any regard to their structure or real nature. Cancers, it is true, may undergo a colloid change (see "Colloid Cancer"); but it is by no means true that all tumors possessing these soft gelatiniform characters are cancers. The terms "mucoid" or "colloid" applied to a new growth merely imply certain physical and chemical characters, and convey but little information as to its real nature.

Allusion must be here made to a change met with in the muscles in typhoid fever, and occurring under certain other conditions, which was first described by Zenker, and which has been supposed to be somewhat allied to colloid degeneration. This change, when occurring in typhoid, is most marked in the recti muscles of the abdomen, the adduc-

tors of the thigh, and in the diaphragm. The portions of muscle affected are paler than natural, of a reddish-gray or brownish-yellow color, and abnormally friable. Under the microscope, the altered fibres are much swollen, the transverse striation is lost, and the sarcolemma is occupied by a homogeneous, structureless material. This material is exceedingly brittle, and, as usually seen, presents a wrinkled appearance, or is broken up transversely into several irregular fragments. (Fig. 17.) The fibres are never universally affected, but many normal are associated with altered elements. This change neces-

FIG. 17.



A portion of the Soleus Muscle from a Case of typhoid fever. Preparation teased after treatment with Müller's Fluid. $\times 200$. Reduced $\frac{1}{2}$.

sarily impairs the contractile power of the muscle, and it often leads to rupture of some of the fasciculi, and hemorrhage. The new material appears to be readily absorbed, and the lost fibres to be quickly regenerated.

With regard to the nature of the change, but little is known. Although most frequent in typhoid, it occurs occasionally in other severe febrile diseases. It is also described by Cornil and Ranvier as sometimes occurring in muscles in the neighborhood of abscesses, of inflamed bone, and of tumor. Muscles which have been bruised or otherwise injured, whether before or after systemic death, occasionally exhibit a similar change; and Prof. Cohnheim considers that it is probably merely some disturbed form of post-mortem coagulation of the muscle. Whether this be so, or whether the change is due to some abnormal chemical process taking place in the muscle during life, must in the present state of our knowledge remain uncertain.

CHAPTER VII.

LARDACEOUS DEGENERATION.

LARDACEOUS degeneration, which is one of the most important of the degenerative processes, is an alteration in the tissues characterized by the appearance in them of a peculiar homogeneous translucent substance closely allied to albumen, by which their vitality becomes diminished and their functions impaired. It is often known as the *amyloid* change, this name having been applied to it by Virchow, from the supposed resemblance of the new material to cellulose or starch. The term lardaceous originated in the fact that the affected organs have somewhat the appearance of lard or wax, and as being that by which it is perhaps most generally known, it is here adopted.

This form of degeneration is very rarely a primary affection, but almost invariably occurs as the sequel of some other disease. There are two conditions which appear to be especially concerned in its causation—suppuration and syphilis. It is in those diseases which are attended by profuse and long-continued suppuration, such as

chronic diseases of bone, empyema, chronic disintegrative diseases of the lungs, chronic pyelitis, and chronic intestinal ulceration, that the lardaceous change is most frequently met with. It also occurs in the advanced stages of syphilis, but especially in those cases in which there is chronic bone disease or chronic ulceration. In quite exceptional cases it is met with in the absence of either of these conditions.

Nearly every organ and tissue may be the seat of the change; those, however, in which it is especially prone to occur are the *liver*, the *spleen*, the *lymphatic glands*, the *kidneys*, and the *intestines*. It is met with less frequently in the stomach, in the supra-renal capsules, in the pharynx, the œsophagus, in the bladder, prostate, and generative organs, in serous membranes, in the membranes of the brain and cord, and in muscle. It also occasionally affects pathological products, as thrombi, inflammatory exudations, etc. It is rarely limited to one organ, but several organs are almost invariably simultaneously affected by it.

Respecting the nature of the new material which exists in the tissues, the analyses of Kekulé and Schmidt show that it is a nitrogenous substance closely allied to albumen. The conclusions arrived at by these observers are, however, not satisfactory, as they were unable completely to separate the substance from the tissues. More recently, Kühne succeeded in more completely isolating it. He submitted the affected organs to a process of artificial digestion, and inasmuch as the lardaceous substance is not dissolved by digestion with pepsin, it was thus obtained free from the tissues in which it was contained. The result of Kühne's analyses is very similar to those of Kekulé and Schmidt. Dr. Dickinson regards the new substance as fibrin deprived of its alkaline salts. The investigations of Dr. Marcet¹ show that the affected organs are considerably deficient in potash and phosphoric acid, whilst they contain an excess of soda and chlorine. In conclusion it may be stated that, although the precise composition of the lardaceous substance has not yet been determined, the results of the several analyses appear to justify the opinion that it is some modification of albumen.

The most characteristic feature of the lardaceous substance is the peculiar reaction which it gives with iodine, and with iodine and sulphuric acid. If an aqueous solution of iodine—made with the help

¹ See "Report of Committee on Lardaceous Disease," Trans. Path. Soc. Lond., 1871.

of potassium iodide—be applied to a lardaceous organ, the affected portion changes to a deep reddish-brown color. This is not permanent, but gradually passes off, and the part regains its former appearance. If the application of the iodine be followed by the cautious addition of sulphuric acid, a blackish-blue or violet tint is produced. This latter reaction, however, is not easily obtained, considerable nicety being required in the application of the reagents. The following is the method for obtaining it, recommended by Professor Virchow: A dilute aqueous solution of iodine must be allowed to soak well into the tissue, the excess must be poured off, and a single drop of concentrated sulphuric acid gradually added, when a blue or violet color will be produced, either at once or after some time. In the hands of English pathologists this latter reaction has certainly met with but little success; and if the color be obtained, it is by no means satisfactory, and more nearly resembles a black than the blue which has been described. Fortunately, however, the reaction with iodine alone is sufficiently characteristic, and the attempt to obtain the blue by the subsequent addition of sulphuric acid, is therefore quite unnecessary. If the change is at all advanced, the reddish-brown color will be produced by merely pouring the aqueous solution of iodine over the cut surface of the organ; but in slighter degrees of the affection, thin sections must be made with a Valentin's knife, and well washed with water to remove the blood, before the coloration with iodine can be obtained.

Certain other forms of altered albumen exhibit a similar color when treated with iodine, so that this reaction cannot be regarded as absolutely characteristic. Recently M. Cornil has discovered another property of the lardaceous substance, which consists in the deep violet staining which the affected tissues undergo when treated with a solution of methylaniline. This reaction appears to be valuable, inasmuch as the staining is much more permanent than that caused by iodine, and thus is more suited for microscopical purposes; and as the iodine reaction can be obtained with other albuminous bodies, M. Cornil's method is especially valuable as a confirmatory test.

The lardaceous substance usually makes its appearance first in the small arteries, the cells of the intima and of the muscular coat being first affected, then the remaining structures of the artery. When the vessels have become involved the new material appears in the immediately surrounding parts, both in the cells and in the intercellular substance. The change may thus involve the whole organ, or it may be limited to certain portions. In the spleen, for example, it is fre-

quently limited to the Malpighian corpuscles; and in the liver to the cells in the more immediate vicinity of the hepatic artery.

The alterations produced in the tissues by this degeneration are very characteristic. The cells gradually increase in size, they lose any irregularities in their contour, and become rounder and more regular in shape, their nuclei disappear, and the whole cell is converted into a structureless homogeneous body which has a peculiar translucent glistening appearance. (Fig. 18, *a*.)

FIG. 18.



Lardaceous Liver Cells. *a.* Single cells.
b. Cells which have coalesced. $\times 300$.
(Rindfleisch.)

If the cells are in close contact many of them may coalesce, and their distinctive boundaries thus become obliterated. (Fig. 18, *b*.) The intercellular substance in the same way acquires a homogeneous glistening appearance. The walls of the small arteries—in which, as already stated, the change usually commences—become considerably thickened, the cells of the muscular coat enlarge and ultimately coalesce, the calibre of the vessel becomes diminished, and the circulation through it is consequently impeded. (See Fig. 20.)

Organs in which this change is at all advanced, present features so characteristic that its nature can be readily recognized by the naked eye. They are usually considerably increased in size; their absolute weight is increased, and also their specific gravity; their surface is smooth, and the capsule tense and stretched; their consistence is firm and somewhat elastic. On section they exhibit a peculiar homogeneous, glistening, translucent appearance, somewhat resembling wax or glue. Owing to the diminished calibre of their bloodvessels and to the pressure exercised by the new material, they contain but little blood, and hence are always pale in color. Although the above characters are often sufficiently marked, they should always be confirmed by the application of iodine or methylamine to the cut surface of the organ. In slighter degrees of the affection, when the physical characters are but little altered, the application of these reagents may become necessary in order to discover the presence of the new substance.

The effect of lardaceous degeneration is to impair or even to completely destroy the nutrition and function of those organs which are affected by it. This is owing to two causes—the obstruction offered to the circulation, and the injurious influence of the new material upon

the vitality of the affected cells. The obstruction to the circulation, which results partly from the diminution in the calibre of the small arteries, and partly from the general pressure exercised by the new substance, causes an insufficiency in the supply of arterial blood. As a consequence of this, the cells tend to undergo fatty metamorphosis, which indeed is frequently associated with the lardaceous change. As this form of degeneration is almost invariably secondary to some grave constitutional state, it can rarely be looked upon as in itself a cause of death, although it may materially hasten, and even determine, the fatal termination.

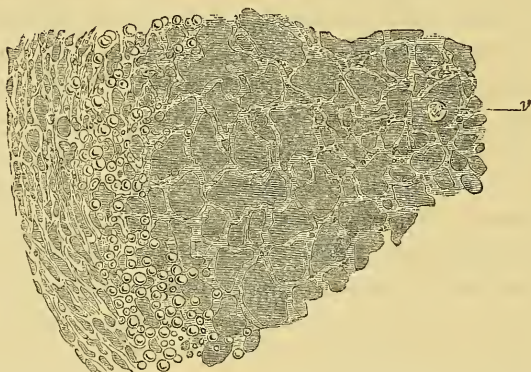
Having thus described the nature of the lardaceous substance, and the way in which it makes its appearance in the several tissues of an organ, it remains to consider the source from which it is derived. The disease has usually been regarded as an infiltration, as the deposition in the tissues of some new material derived from the blood. This view is based upon the way in which the several tissues of an organ are affected, the change usually commencing in the small nutrient bloodvessels, and extending from them to the surrounding parts; upon the general character of the affection, several organs being simultaneously involved; and upon the fact that the disease is almost invariably secondary to chronic suppuration or syphilis. The existence, however, of any albuminoid substance in the blood which resembles the lardaceous material in its chemical reactions, has never been made out even in the most marked cases of the disease. This fact must therefore negative the supposition that it is a simple infiltration. If the new material be derived from the blood at all, it must undergo some chemical change subsequently to its deposition in the tissues. Dr. Dickinson considers that it is dealkalized fibrin, which is deposited in consequence of the loss of the alkali which it normally contains. This loss of alkali he attributes to the chronic suppuration which usually precedes the disease, pus containing large quantities of potassium and sodium salts. He consequently terms the disease "depurative infiltration."¹ Whatever be the exact nature of the change, it is probably due to some abnormal state of the blood, although whether the new substance found in the organs is a deposition, or an altered condition of the albumen of the tissues due to the altered blood, must for the present remain uncertain.

¹ "Medico-Chirurgical Transactions," vol. 1.

Lardaceous Degeneration of the Liver.

The liver is one of the most frequent seats of the lardaceous change, and here, as in other parts, it probably commences in the small nutrient bloodvessels, although the alterations are much the most marked in the hepatic cells. If a liver be examined in the earlier stages of the affection, and the iodine solution applied to thin washed sections of the organ, it will be found that the characteristic staining is limited to certain portions of the lobules—viz., to those which are situated between their external and central parts. This intermediate portion corresponds with the distribution of the hepatic artery, and the ramifications of this vessel, together with the hepatic cells situated in their vicinity, are the first to become affected. (Fig. 19.) As the change

FIG. 19.



Lardaceous Liver. A portion of one lobule, showing the enlargement and fusion of the hepatic cells, and the greater implication of the intermediate zone of the lobule. At the more external portion of the lobule are seen several fat cells, a certain amount of fatty infiltration being associated with the lardaceous change. *v.* Hepatic vein. $\times 100$.

advances the whole lobule may ultimately become involved. The alterations in the hepatic cells are very characteristic. They are much enlarged, irregular in outline, their nuclei are imperceptible, and many of them are fused together into irregular-shaped masses. (See Fig. 18.)

The earliest seat of the lardaceous change thus differs from that of the fatty. In fatty infiltration it is the most external portion of the lobule in which the fat accumulates—that which corresponds with the distribution of the portal vein. (See Fig. 8.) It differs also from that pigmentation of the hepatic cells, resulting from mechanical con-

gestion, which takes place in the most central portion, around the hepatic vein. (See "Nutmeg Liver.") Thus in each hepatic lobule three zones may be distinguished: an external one, which is the chief seat of the fatty change; a central one, which is the chief seat of the pigmentary change; and an intermediate one, which is the chief seat of the lardaceous change. These three zones, indeed, may frequently be recognized by the naked eye, the pale opaque external one contrasting strongly with the intermediate one which is translucent, and with the darker central one. In the most advanced stages of the disease, however, both the external and central portions of the lobule may become involved, and the cut surface present an almost uniformly homogeneous appearance.

The lardaceous liver is increased in size, often very considerably so; it may be so large as almost completely to fill the abdominal cavity. The enlargement is uniform, and hence the natural configuration of the organ is but little altered. Its weight is increased, and also its specific gravity. Its edge is rounded, the surface is smooth, and the capsule appears tense and stretched. The consistence is firm and elastic. The cut surface is dry, bloodless, smooth, translucent, and waxy-looking, and of a pale reddish-gray or dirty yellow color. If the change is very far advanced, the tissue may be perfectly homogeneous, all distinction between the individual lobules being lost. In other cases the lobules are distinctly mapped out; they are enlarged, and the external zone may be of an opaque yellowish-white color owing to the presence of fat. This association of the fatty and lardaceous changes is exceedingly common. Lardaceous degeneration does not obstruct the portal circulation, and hence does not cause ascites. It impairs the vitality of the hepatic cells, and thus interferes with the functions of the organ.

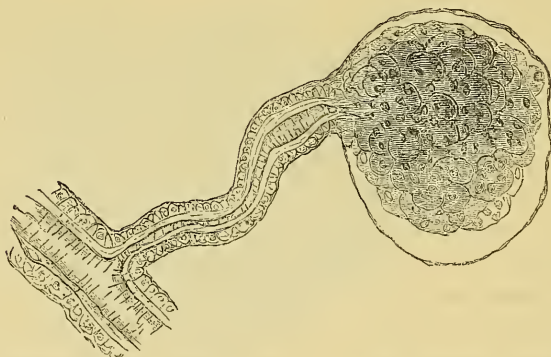
Lardaceous Degeneration of the Kidneys.

The kidneys are very liable to be involved in the lardaceous change, and here it is the smaller bloodvessels which are more especially affected. It may constitute in them the primary lesion, or it may occur subsequently to inflammatory conditions implicating the secreting and interstitial structures. As a primary change it is an important variety of Bright's disease.

The process usually commences in the tufts of vessels which form the Malpighian bodies, the walls of which become thickened by the

new material, so that the tufts are increased in size. It then involves the small afferent arteries, and ultimately the vasa efferentia and the arteriolæ rectæ which run through the medullary portion of the organ. The changes produced in the vessels are very characteristic. Their walls are considerably thickened, and their calibre is so much diminished that the smallest ones cannot be artificially injected. This thickening of the walls of the vessels is mainly owing to alterations in their muscular coat, and especially to the cells of the circular muscular layer. These cells are much increased in size, they are more or less globular in shape, and many of them have lost their distinctive outlines. The longitudinal muscular fibres and the most internal coat of the vessel are often seen as one homogeneous, glistening, structureless layer. (Fig. 20.) After the vessels have become affected, the intertubular

FIG. 20.



Lardaceous Degeneration of a Malpighian Tuft and small Artery of the Kidney. Showing the thickening of the walls of the vessel, the enlargement of the cells of the circular muscular coat, and the homogeneous layer formed by the intima and longitudinal muscular fibres. $\times 200$, reduced $\frac{1}{2}$.

tissues of the cortex are involved, and in some cases the epithelium of the tubes also undergoes the lardaceous change. In the earlier stages of the process, however—if the organ is not the seat of any other morbid change—the tubes and their lining epithelium present a perfectly natural appearance. Many of them contain pale hyaline casts, which also appear in the urine. These, however, are probably simply exudation products; although, from the reaction they occasionally exhibit, it appears that they sometimes consist of the same material as that which permeates the vessels and intertubular structures. As the change proceeds, and the new material increases in amount, the tubes become compressed; and in many places completely obstructed. If

the compression is not uniform, they may dilate and form small cysts. The epithelium, which was at first normal, owing to the interference with its nutrition, ultimately atrophies and undergoes fatty changes. In some cases it appears to be the seat of a catarrhal process, and the tubes are found blocked with the epithelial products. In the later stages of the process there is almost invariably an increase in the intertubular connective tissue.

The first effect of this change is to obstruct the circulation in the cortex. The bloodvessels, diminished in calibre, allow little but the liquor sanguinis to pass through them, the passage of the blood-corpuscles being to a great extent prevented: hence the pallor of this portion of the organ. The arterial walls are so altered that fluids and albumen readily permeate them; and thus is produced the large quantity of urine, loaded with albumen, which characterizes the earlier stages of this affection. As the change proceeds, and the tubes become obstructed, the urine diminishes in quantity. The excretion of urea is less interfered with than in other forms of Bright's disease, and hence symptoms due to its retention seldom occur. Tube casts are rarely numerous; they are for the most part hyaline or finely granular, though sometimes they are covered with fatty epithelium.

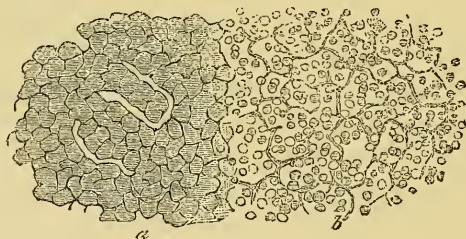
In the earlier stages of the affection, the cortex of the kidney is merely rather paler than natural, and perhaps somewhat firmer in consistence; but otherwise it presents no abnormal appearance. It is only upon the application of iodine to the cut surface, or to thin washed sections of the organ, that its diseased condition becomes evident. When this test is employed, the Malpighian bodies at once become apparent as minute red points scattered through the cortex. As the disease advances, the size of the organ increases; the enlargement, however, is principally confined to the cortex. The surface is smooth, and the capsule separates readily. The enlarged cortex is remarkably pale and anæmic, and has a peculiar translucent, homogeneous, wax-like appearance. Its consistence is hard and firm. A few scattered vessels may be seen on the surface, and the bases of the pyramids sometimes exhibit an increased amount of vascularity. If iodine be poured over the cut surface, the Malpighian bodies and the arteries of the cortex become mapped out almost as clearly as in an artificial injection. The enlarged Malpighian bodies indeed may usually be seen as glistening points before the iodine is applied. Frequently, the homogeneous appearance of the cortex is interrupted by minute, opaque, yellowish-white lines and markings; these are

produced by the fatty changes in the epithelium of the tubes, which so commonly occur in the later stages of the affection. Ultimately the capsule becomes more or less adherent, and slight irregular depressions make their appearance upon the surface of the organ: the latter are due to atrophic changes in some of the tubes. If, as is usually the case, the process is associated with an increase in the intertubular connective tissue, the atrophy of the organ will be more marked. (See "Interstitial Nephritis.")

Lardaceous Degeneration of the Spleen.

Lardaceous degeneration of the spleen is met with in two forms—one in which the disease is limited to the Malpighian corpuscles—the "Sago Spleen," and the other in which the pulp appears to be chiefly implicated. The former is much the more common condition. In it the Malpighian corpuscles undergo the lardaceous change, and become converted into translucent wax-like bodies, much like boiled sago; hence the name. The process commences in the small arteries of the corpuscle, and then the lymphatic cells of which the corpuscle is made up are involved; they increase in size, become more irregular in outline, many of them coalesce, and ultimately the whole is converted into a pale, firm, translucent, glistening mass. (Fig. 21.)

FIG. 21.



Lardaceous Degeneration of the Spleen—"Sago Spleen." A portion of one of the altered Malpighian corpuscles, *a*, with the adjacent normal splenic tissue, *b*. Showing the increase in size, and in many parts, the coalescence of the cells, of which the corpuscle is composed. $\times 200$.

The sago spleen is more or less enlarged; its weight and density are also increased. The cut surface is smooth, dry, and studded all over with small glistening sago-like bodies, varying in size from a millet to a hemp-seed, which are stained a reddish-brown color by the iodine solution. These may become so large as to occupy a large

portion of the organ, although in earlier stages of the affection they are so minute that they can only be seen in thin sections of the tissue.

In the other variety of lardaceous spleen, the pulpy parenchyma between the corpuscles is principally affected. This is probably merely an advanced stage of the former condition, in which the disease extends from the corpuscles to the surrounding pulp; the whole organ being ultimately involved. Under these circumstances the organ often attains a considerable size, much larger than is met with in the sago spleen. It is remarkably hard and firm, and the capsule is tense and transparent. On section it presents a dry, homogeneous, translucent bloodless surface, of a uniform dark reddish-brown color.

Thin sections can be readily made with a knife, the organ cutting like soft wax. The corpuscles are not visible as in the former variety, being probably obscured by the surrounding pulp.

Lardaceous Degeneration of Lymphatic Glands.

In the lymphatic glands the process much resembles that in the spleen. The small arteries in connection with the follicles of the gland are the earliest seats of the change; and from these it extends to the lymphoid cells. The follicle thus becomes ultimately converted into a small homogeneous mass.

The glands are enlarged, and on section the minute wax-like bodies can often be seen scattered through the cortex. The cut surface is smooth, pale, and translucent.

As these glands are largely concerned in the formation of the blood-corpuscles, their implication in the lardaceous change must to a large extent aid in producing the emaciation and anæmia which characterize this affection. The same is true of the spleen, which is usually simultaneously involved.

Lardaceous Degeneration of the Alimentary Canal.

The whole of the alimentary tract may be the seat of the lardaceous change, and here it assumes an important aspect from the deleterious influence which it exercises upon the absorbent and secreting processes, and from the consequent impairment of the general nutrition which results. The disease, however, in this situation is very apt to escape observation, as it produces but little alteration in the appearance of the parts. The mucous membrane may look some-

what pale, translucent, and œdematous, but otherwise to the naked eye nothing is discoverable. It is only upon the application of iodine to the washed mucous surfaces that the nature of the change becomes apparent. In the small intestine—which is perhaps the part most commonly affected—the effect of the application of iodine is very characteristic. A number of small reddish-brown points appear over the whole surface of the membrane; these correspond to the intestinal villi, the arteries and capillaries of which have undergone the lardaceous change. In the stomach and œsophagus the vessels are mapped out in a similar manner by the iodine solution. The change in the intestine gives rise to serous diarrhœa, this being probably due to an increased permeability of the degenerated walls of the vessels.

The Corpora Amylacea.

The corpora amylacea or “amyloid bodies,” so frequently met with in the nervous system, in the prostate, and in other parts, have usually been looked upon as more or less allied to the lardaceous substance; there appears, however, with the exception of a certain similarity in their behavior with iodine and sulphuric acid, to be no connection between them.

They are round or oval bodies, formed of a succession of concentric layers, and are often changed to a deep blue color by iodine, thus

bearing, both in their structure and chemical properties, the strongest resemblance to granules of vegetable starch. (Fig. 22.)

Sometimes, however, the blue is only exhibited after the subsequent addition of sulphuric acid, and thus a resemblance is shown to the lardaceous substance. They vary in size from microscopic granules to bodies which are distinctly visible to the

naked eye; sometimes being as much as one or two lines in diameter. The larger ones are usually formed by the conglomeration of the smaller granules, which are often inclosed by a common envelope.

They occur especially in conditions of atrophy or softening of the nervous system; the ependyma of the ventricles, the white substance of the brain, the choroid plexus, the optic nerve and retina, and the spinal cord being their favorite seats. The larger forms are met with most frequently in the prostate. The prostate of nearly every adult

FIG. 22.



Corpora Amylacea from the Prostate. (Virchow.)

contains some of these bodies; and they may accumulate here to such an extent as to form large concretions. They are occasionally met with in the lungs, and in mucous and serous membranes.

As has been said, they usually exhibit a bright blue color upon the application of iodine alone, although in some cases not until the subsequent addition of sulphuric acid. Many of them, however, are colored green, or even brown by these reagents. The green is due to their admixture with nitrogenous matters, which give a yellow color with iodine, and hence the combination yields a green. The greater the amount of nitrogenous matter the more brown does the color become.

From the laminated structure of these bodies they would appear to be formed by the gradual precipitation of some material, layer by layer, upon the surface of pre-existing particles. The nature of the material, however, does not appear to resemble that of the substance met with in lardaceous degeneration. The two processes are so essentially different, both in the circumstances under which they occur and in the characters and seat of the morbid products, that they cannot be looked upon as in any way analogous. Lardaceous degeneration is a general change, whereas the formation of the corpora amylacea is evidently of a local nature. The latter is often preceded by those local atrophic changes associated with advanced life, and appears to consist in the deposition of some starch-like material, probably liberated in the tissues themselves, upon any free body which may exist in its vicinity.

The corpora amylacea, especially those occurring in the choroid plexus and in the lateral ventricles, are very liable to become calcified, and they then constitute one form of "brain sand," which is so often met with in these situations.

CHAPTER VIII.

CALCAREOUS DEGENERATION.

CALCAREOUS degeneration—or as it is more commonly called *calcification*—consists in the infiltration of the tissues with calcareous particles. Physiologically, an infiltration of calcareous particles takes place in the formation of bone, in which lime and magnesian salts are deposited in the fibrous or cartilaginous matrix. This physiological is precisely similar to the pathological process. It is important, however, to distinguish simple calcification from ossification. In the latter there is not only a deposition of lime salts, but an *active* change in the tissue itself—a proliferation of the cellular elements, an intimate union of the calcareous matters with the tissue, and the formation of a true osseous structure in which the calcareous particles are not visible. Calcification, on the other hand, is a purely *passive* process: there is no increased nutritive activity of the part, no multiplication of elements, no alteration of the structure, but merely an infiltration with calcareous particles.

An infiltration and deposition of calcareous substances occurs under two opposite conditions: one—in which there is an absolute increase in the amount of these constituents in the blood, and a portion of the excess becomes deposited in the tissues; the other—in which there is no such increase, but the deposition takes place owing to some alteration in the tissue itself. That the calcareous particles are in all cases brought to the part, and are not simply those normally contained in it which have become precipitated, is shown by the fact that their quantity greatly exceeds that of healthy tissue.

An absolute increase of the saline constituents in the blood, and the deposition of the excess in the tissues, is much the less frequent form of calcification. It occurs in some forms of softening of bone, especially in extensive caries and osteomalacia. In these diseases the lime salts are removed from the bone, returned into the blood, and some of them deposited in other tissues. In such cases the calcification is usually more or less general—many organs being simultaneously involved. In osteomalacia it is not uncommon to find the kidneys,

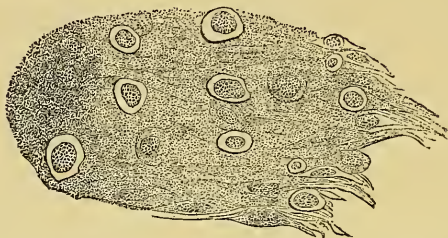
the lungs, the stomach, the intestines, and even the dura mater and liver, infiltrated to a greater or less extent with lime salts. The deposition takes place in the tissue immediately surrounding the blood-vessels, through the walls of which the calcareous matters transude;—thus, in the lungs the seat of the change is the interlobular tissue; in the stomach, the stroma between the glands; and in the kidney, the tubuli uriniferi and the intertubular tissue. Analogous to this form of calcification is the deposition of the excess of urate of soda which takes place in gout.

In the great majority of cases, however, calcification is a *local* change, depending not upon any alteration in the composition of the blood, but upon changes in the tissues themselves, owing to which some of the saline matters which are normally held in solution in the blood are deposited in them. The alteration in the tissues consists in some enfeeblement of the nutritive processes, associated with a diminution in the amount of blood, and a retardation of its circulation. Calcification is therefore very frequent as a senile change, and is especially common in the arteries of old people. (See “Calcification of Arteries.”) It also occurs under other circumstances where tissue changes are very feeble, as in thrombi, in the caseous masses so common in the lungs and lymphatic glands, in atheromatous arteries, and in non-vascular tumors. Respecting the cause of the deposition of the calcareous substances—it is probably partly due, as stated by Rindfleisch, to the stagnation of the nutritive fluids in the part, owing to which the free carbonic acid, which appears to hold the salts in solution, escapes, and they are consequently precipitated; and partly to the non-assimilation of these fluids by the enfeebled elements of the tissue.

The calcareous particles make their appearance both within the cells and in the intercellular substance; they are much more frequent, however, in the latter situation. They are seen at first as fine molecules scattered irregularly through the intercellular substance. (Fig. 23.) They are characterized, when viewed by transmitted light, by their opacity, dark black color, and irregular outline, and also by their solubility in dilute mineral acids. They gradually increase in number until ultimately large tracts of tissue may be converted into an opaque calcareous mass, in which the cells are inclosed and can no longer be recognized. These larger masses have a sharp black irregular outline, and as the calcification becomes complete, acquire a homogeneous, glistening, semi-transparent appearance. The cells

themselves are much less frequently infiltrated, being usually merely inclosed and obscured by the calcified intercellular substance. Cal-

FIG. 23.



A Calcified Sarcomatous Tumor. Showing the minute calcareous particles scattered through the intercellular substance. To the left of the figure they are so abundant as to almost completely obscure the cells. $\times 200$.

careous particles may, however, make their appearance in the protoplasm, and, gradually increasing, convert the cell into a homogeneous calcareous body.

The calcareous matters consist, for the most part, of lime and magnesian salts, especially the phosphates and carbonates. If the latter are present, the addition of a little dilute hydrochloric acid is followed by the appearance of numerous minute air bubbles in the tissue, owing to the liberation of carbonic acid. In those cases in which calcification is associated with retained gland secretions, the calcareous matters will consist of the specific gland salts.

A part which has become calcified undergoes no further change; its vitality is completely destroyed, and it remains as an inert mass. In this respect calcareous differs from fatty degeneration. In the latter, subsequent changes invariably take place; the part either softening, caseating, or becoming the seat of calcification itself. It differs also in its effect upon the tissue. The structure of the affected part is not destroyed, and there is no annihilation of histological elements, such as occurs in fatty degeneration. The tissue is simply impregnated with calcareous matters, which have no other effect upon it than to render it inert; its vitality is destroyed, but its structure—in so far as the calcification is concerned—remains unaltered. If the saline matters are dissolved out with a little dilute mineral acid, the structure of the part may be again recognized, unless, indeed—as is so often the case—it has been destroyed by any antecedent change.

Calcification must thus be looked upon in many cases as a salutary lesion, the impregnation with calcareous matters preventing subsequent

changes in the part. This is especially the case when it is secondary to other forms of degeneration. It is often the most favorable termination of the large class of fatty changes, as is exemplified by the calcification of caseous products in the lungs, and of many new formations. It may, on the other hand, under certain circumstances, be attended with most deleterious consequences, as is the case when it affects the arterial system.

Calcification of Arteries.

Calcification of arteries, like fatty degeneration, may be a *primary* or *secondary* affection. As a secondary change it constitutes one of the terminations of the atheromatous process, and as such is constantly met with in the aorta and its branches, and in many other situations. (See "Atheroma.")

Primarily calcification is essentially a senile change, and is the result of that impairment of the nutrition of the arteries which exists in advanced life. It is associated with atrophy of the arterial tissues, and in some cases with fatty degeneration. The change is a more or less general one, and when occurring in one part is met with in others. It usually occurs in vessels of medium size, the arteries of the upper and lower extremities and of the brain being those most commonly affected. Its most common seat is the middle coat, where it commences in the muscular-fibre cells. The calcareous particles, which are deposited from the vasa-vasorum, make their appearance at first around and within the nucleus, and gradually increase until they fill the cell, which becomes converted into a small calcareous flake. The process may go on until the muscular coat is completely calcified, or it may be limited to isolated portions of the coat, giving rise to numerous calcareous rings and plates which are irregularly distributed throughout it. From the muscular it may extend to the external and internal coats, until ultimately the vessel becomes calcified throughout.

The vessel thus calcified loses its elasticity and contractility; its lumen is diminished, and it is transformed into a hard, rigid, brittle tube. This condition is common in the external iliac and in the vessels of the lower extremity, where it is a frequent cause of senile gangrene. (See "Senile Gangrene.")

CHAPTER IX.

PIGMENTARY DEGENERATION.

PIGMENTARY Degeneration, or Pigmentation, consists in an abnormal formation of pigment in the tissues. All true pigments are derived from the coloring matter of the blood. Physiologically, many of them are eliminated by the kidneys and liver ; others are deposited in the tissues and there remain permanent. The choroid coat of the eye and the skin of the negro are well known examples of tissues in which there is this permanent accumulation of pigment. The cells in these situations appear to be endued with a special power to abstract the coloring matters from the blood, and to store them up in their interior, where they undergo certain chemical changes and become converted into pigment.

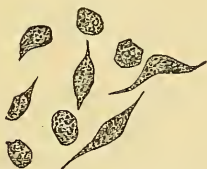
In the pathological process, also, the pigment is derived from the same source, although its presence in the tissues is rarely dependent upon any abnormal secreting powers in their cellular elements, but is usually the result of certain changes in the circulation or in the blood-vessels, owing to which the coloring matter of the blood escapes and infiltrates the surrounding parts. This escape of hæmoglobin may be owing to rupture of the vessels themselves, or to conditions of congestion or stasis in which the blood-corpuscles and liquor sanguinis pass through their walls. In either case the hæmoglobin will permeate the tissues and ultimately be converted into pigment. Rupture of the vessels and the direct extravasation of blood, is, however, the most common antecedent of the pigmentary change. Soon after the extravasation has taken place, the hæmoglobin escapes from the red blood-corpuscles, either by exudation or by destruction of the corpuscle, and, mixed with the liquor sanguinis, infiltrates the surrounding tissues. In other cases the process takes place without any solution of continuity in the walls of the vessel. This frequently occurs in conditions of inflammatory stasis and mechanical congestion, in which the red corpuscles pass through the walls of the capillaries, and some of the hæmoglobin is also liberated from the corpuscles within the vessels, from which it transudes, dissolved in the liquor sanguinis, without

rupture having taken place. In whichever of these ways the hæmoglobin is derived, it infiltrates the tissues, staining both the cells and the intercellular substance a yellowish or brownish-red color. It is taken up, however, more readily by the cells than by the intercellular substance or by membranous or fibrous structures. In addition to this formation of pigment from dissolved hæmoglobin, the red corpuscles themselves may penetrate the adjacent cells and there become converted into pigment. Some of the corpuscles also, after their escape from the vessels, may shrivel up and become pigment granules. It is probable that in some cases these changes and the subsequent formation of pigment may take place within the vessels.

After the hæmoglobin has remained in the tissue for some length of time, it undergoes certain changes: It becomes darker and more or less granular, minute reddish-brown or black granules and crystals make their appearance both in the cells and in the intercellular substance, and these may gradually increase and form larger masses. This change in the hæmoglobin is a chemical one, and the substance into which it is converted is *hæmatoidin*. Hæmatoidin appears to be closely allied to the coloring matter of the bile, cholepyrrhin, which is also a derivative of hæmoglobin. It exhibits similar reactions when treated with concentrated mineral acids, displaying the same variations of green, blue, rose, and yellow colors. It is insoluble in water, alcohol, ether, and in dilute mineral acids and alkalis; it is soluble in the caustic alkalis, giving a red color. It contains more carbon than hæmoglobin; and it also contains iron.

The granules of hæmatoidin vary in size from the smallest particles to masses as large as a red blood-corpuscle. (Fig. 24.) The larger

FIG. 24.



Cells containing pigment. From a melanotic sarcoma of the liver. $\times 350$.

FIG. 25.



Hæmatoidin crystals. (Virchow.)

ones are round, or more commonly irregular in shape, and have a sharp defined border. Their color varies from yellow, red, and brown, to black. These variations appear to depend upon the age of the granules and the tissue in which they are formed; the older they

are the blacker they become. The smaller granules are usually dull and opaque; the larger ones, however, often present a more or less glistening appearance. The crystals of hæmatoidin are opaque rhombic prisms, usually of a beautiful yellowish-red or ruby-red color, sometimes approaching to brown or black. They may also occur as little plates and fine needles, but these are less common forms. (Fig. 25.) They are in most cases so small that considerable care is required to recognize their crystalline nature under the microscope, and they may easily be overlooked as merely irregular granular masses. In some cases, however, they attain a larger size. They are more or less transparent, and present a shining, strongly refracting surface.

Whether the hæmoglobin is converted into granular or crystalline hæmatoidin appears partly to depend upon the tissue in which it is situated, the crystals being exceedingly common in some situations, as in the brain and ovaries, whereas in others, as mucous membranes, only the granules are met with. Both the granules and crystals are characterized by their durability and by their great powers of resistance; when once formed they undergo no further change.

Those forms of pigment—both granular and crystalline—which are of an intensely black color, have been supposed to consist of a substance which differs in chemical composition from hæmatoidin, and which has been called *melanin*. There appears, however, to be no foundation for such a distinction. Melanin is probably merely hæmatoidin which has become more or less altered by age. It is endued with greater powers of resistance, being less readily soluble in reagents than the more recently formed hæmatoidin, and it contains more carbon.

Pigmentation, although one of the most common forms of degeneration, is of comparatively little importance as a morbid process. The mere existence of pigment within and between the histological elements of the tissues, has in itself but little influence upon their vitality and functions. The atrophy and impairment of function which so frequently accompany it, must rather be looked upon as the result of those conditions upon which the formation of the pigment depends, than as in any way owing to the presence of the pigment itself.

As evidence of other antecedent conditions, pigmentation assumes a more important aspect. The pigment being derived from extravasated hæmoglobin, in whatever situations it occurs, it is usually to be

looked upon as the result of some alteration in the circulation or in the bloodvessels, owing to which the escape of the coloring matter is permitted. Exceptions to this exist, however, in the case of certain pigmented new formations, in which the presence of the pigment appears to be mainly owing to the selective power of the cells; these, like those of the choroid, separating the coloring matter from the blood. It is those growths which originate in tissues normally containing pigment, as the choroid and rete mucosum, which are most frequently melanotic. (See "Melanotic Sarcoma.") In Melanæmia, again, the large quantities of pigment which exist in the blood, are probably the result of a local formation—for the most part by the spleen. Lastly, in Addison's disease, the pathology of the pigmentation of the skin is at present involved in obscurity.

Pigment is often the only evidence of a former extravasation. This is frequently the case in cerebral hemorrhage, where the crystals of hæmatoidin may be all that remains to indicate that rupture of the capillaries has taken place. In the ovaries, also, the slight hemorrhage which follows the escape of the ovum at each menstrual period is marked by the formation of pigment which constitutes the "corpus luteum." In mechanical congestion and inflammation, again, the consequent pigmentation may be the principal evidence of the former existence of these conditions: this is especially seen in pigmentation of the mucous membrane of the stomach and intestines. The formation of pigment is thus, with the few exceptions above named, the result of some antecedent change in the bloodvessels or circulation; and its presence in the tissues appears to be little more than a testimony to the existence of those processes upon which its formation depends.

FALSE PIGMENTATION.—There are certain forms of discoloration of the tissues which are not due to the presence of hæmatoidin: these must be distinguished from true pigmentation. The most important of them, and that which is most closely allied to the process already described, is the staining of the tissues with the coloring matter of the bile, which is itself a derivative of hæmoglobin, and is, as before stated, very analogous to hæmatoidin. This yellow staining may affect nearly all the tissues, constituting "jaundice;" or it may occur in the liver alone, from local obstructions to the small bile-ducts, as is often seen in cirrhosis of that organ. In these cases, however, there is merely the staining of the tissues with the coloring matter of the bile and no subsequent conversion of this pigment.

The discoloration caused by the long-continued use of the salts of

silver must also be distinguished from pigmentation: the color here is due to the deposition of the silver in the tissues. The black color of gangrenous parts, and that sometimes produced by the effusion of large quantities of blood into the tissues, must again not be confounded with pigmentation. The discoloration in these cases is the result of the action of the sulphuretted hydrogen upon the coloring matter of the blood. The greenish-black discoloration so often seen on the surface of the liver, kidneys, and other abdominal organs after death, is in the same manner due to the intestinal gases. Lastly, the minute particles of inhaled carbon, which are always met with in the lungs, must be distinguished from true pigment.

Pigmentation of the Lungs.

In no organ is pigment met with so frequently and in such large quantities as in the lungs, and here much discussion has arisen as to its nature and origin. The lungs normally contain more or less pigment, the amount of which gradually increases with advancing age—the lungs of infants and young children being almost free from it, whereas those of adults invariably contain it in considerable quantities.

This normal pigmentation of the lungs is principally due to the presence of carbon, and not to that of true hæmatoidin-pigment. The carbon—which is derived from the incomplete combustion of wood, coal, and other substances, and is always present in varying quantities in the atmosphere—is inhaled, and the minute particles pass into the finest bronchial tubes. Having entered the bronchi, many of them are taken up by the mucus-corpuseles, where they may be seen as small black granules within the cells. These may readily be observed in the cells of the grayish-black sputum which is so frequently expectorated in the early morning. Much of the carbon thus inhaled is eliminated by expectoration; many of the particles, however, pass into the air-vesicles, and here their removal by this means being less readily effected, they gradually penetrate the pulmonary substance, and make their way into the alveolar walls and interlobular tissue. It is in these situations that most of the pulmonary pigment is found, and there it may be seen either within the connective tissue-cells, or lying free amongst the fibres. (Fig. 26.)

The means by which the particles of carbon penetrate the walls of the air-vesicles, and make their way into the inter-alveolar tissue, has recently been explained by the researches of Dr. Klein on the histo-

logy of the lungs.¹ Dr. Klein finds that the branched connective-tissue cells of the alveolar walls send a process, or a greater or less portion of their body, between the epithelial cells of the alveolus into the alveolar cavity. As these connective-tissue cells lie in the serous

FIG. 26.



Pigmentation of the Lung. From a woman æt. sixty-five, with slight emphysema. Showing the situation of the pigment in the alveolar walls, and around the bloodvessel *v*. $\times 75$.

canals, which constitute the commencement of the perivascular lymphatics, it is easy to understand how these openings in the alveolar walls (pseudostomata) may become sufficiently distended to allow cells and other substances to pass through them from the alveolar cavity into the inter-alveolar tissue. When once the carbon has made its way into the inter-lobular tissue, some of it is taken up by the fixed cells in this situation, whilst that which is not thus detained passes on to the lymphatic glands, where the black particles are also visible.

Closely allied to this physiological pigmentation of the lung from the inhalation of carbon, are those morbid conditions which result from the inhalation of particles of coal, stone, iron, and other substances—of which the lungs of miners, stonemasons, and grinders afford frequent examples. Here also minute particles enter the bronchi, penetrate the walls of the alveoli, and are deposited principally in the interstitial tissue. In the case of miners—in which this is most common—the particles of coal enter the lungs in such large quantities as to give to them a uniform dark blue color. In stonemasons, grinders,

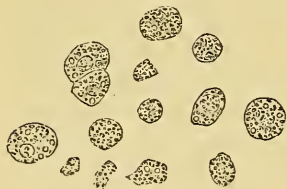
¹ "On the Anatomy of the Lymphatic System of the Lungs," by Dr. E. Klein. Proceedings Royal Society, No. 149. 1874.

etc., the lungs also become deeply pigmented, although to a less extent than those of miners.

The black color of the lungs in these cases, however, is not entirely due to the presence of the inhaled substances, but partly to that of true hæmatoidin-pigment. The inhalation of the irritating particles sets up inflammatory changes in the bronchi and pulmonary tissue, causing chronic bronchitis, chronic catarrhal pneumonia, and a large increase in the fibrous tissue of the lungs, which thus ultimately become consolidated, excavated, tough, and fibrous ("Colliers" and "Knife-grinders' Phthisis," etc.) Owing to these structural changes there is a considerable escape of coloring matter, either from rupture of the capillaries or transudation of serum, and hence a large formation of true pigment; and to this true pigment much of the dark color of these lungs must undoubtedly be ascribed. The lungs of stone-masons and grinders are, like those of miners, deeply pigmented, although to a less degree; but the black color in the former cases cannot be entirely accounted for on the supposition that it is due to the presence of inhaled particles.

Pigmentation of the lungs from the presence of hæmatoidin occurs as the result of many other morbid conditions, many diseases of these organs being attended by the formation of pigment. In chronic phthisis, pigmentation occurs, partly from the obstruction of the inflammatory process, and partly from the

FIG. 27.



Cells from the sputum of acute Bronchitis. Showing the minute granules of pigment within the cells. Some of the cells also contain a few fatty molecules. $\times 400$.

obstruction of the vessels caused by the new growth: lines of pigment are constantly seen surrounding the nodules of consolidation. In acute croupous pneumonia, the blood which is extravasated into the air-vesicles, and which in the early stages gives to the expectoration a rusty or prune-juice color, subsequently becomes converted into pigment, and the sputum becomes of a grayish-black; the pigment granules being visible in the newly-formed cells. The cells met with in the sputum of bronchitis also contain granules of pigment (Fig. 27); and pigmentation plays an important part in the condition of the lungs known as brown induration. (See "Brown Induration of the Lungs.")

Pigment in the lung usually occurs as black irregular granules; it is rarely met with in a crystalline form. In all cases in which it is

found in any quantity in the lung, it is also found in the bronchial glands. It is taken up by the lymphatics and, like the inhaled carbon, it becomes arrested in its passage through these glands, where it remains permanently.

CHAPTER X.

TISSUE-CHANGES IN PYREXIA.

It is proposed in the present chapter to allude very briefly to those alterations in the tissues which are met with in certain pyrexial diseases, to which have been applied the term "parenchymatous" or "granular degeneration," "albuminous infiltration," "acute" or "cloudy swelling."

It is well known that in most diseases which are accompanied by a considerable elevation of the bodily temperature, and especially in those in which the blood has undergone marked changes, the organs and tissues are found much altered after death. The diseases in which such alterations are most frequently met with are pyæmia, erysipelas, typhus, typhoid, and other acute specific fevers, and acute rheumatism. They also occur in other diseases which are attended by considerable pyrexia, but they are most marked in the specific fevers, and appear to depend more upon the alteration of the blood in these fevers than upon the amount of elevation of the bodily temperature. The organs in which the alterations principally occur are the liver, the kidneys, the heart and muscles, and the lungs. Sometimes the changes are much more advanced in some organs than others, owing probably to differences in the local circulation.

The physical characters of the altered organs vary. It may, however, be stated generally that the organs are more or less swollen and opaque, somewhat diminished in consistence, and abnormally friable. Their vascularity is in some cases diminished, in others slightly increased. When examined microscopically, the cellular elements are found to be increased in size, and their protoplasm is markedly granular, so that, in some cases, the nucleus is so much obscured as to be indistinguishable. (Fig. 28.) The granular condition of the proto-

FIG. 28.



Liver from a case of Acute Rheumatism with high Temperature. Showing the swollen and granular condition of the liver-cells. In many of the cells the nucleus is so much obscured as to be almost indistinguishable. $\times 200$.

plasm appears in most cases to be due to albuminous particles, inasmuch as it disappears upon the addition of dilute acetic acid. In other cases, however, in which the change is apparently more advanced, many of the granules are larger, insoluble in acetic acid, but soluble in ether, and obviously fatty.

The Liver.—Here the change is usually met with in its most marked degree. The organ is slightly enlarged, abnormally soft and friable, and the cut surface has a dull opaque

look, being paler than natural. The liver cells are swollen and granular, and in many cases contain fatty particles. (See Fig. 28.)

The Kidneys.—In the kidneys the change affects especially the cortex. This is swollen, opaque, and friable. The Malpighian bodies and the pyramids are usually abnormally vascular, and thus contrast with the pale cortex. The epithelium in the tubes of the cortex presents the appearances above described. These are precisely similar to those met with in the earlier stages of tubal nephritis.

The Heart.—The alteration produced in the heart consists in slight opacity, pallor, and diminution in the consistence of the muscular tissue. Under the microscope the muscular fibres are seen to have lost their distinct striation and to be finely granular. (Fig. 29.)

FIG. 29.



Muscular Tissue of the Heart, from a case of Severe Typhoid Fever. Showing the granular condition of the fibres and the loss of their striation. $\times 400$.

Such a condition must materially interfere with the contractile power of the organ. A similar change is met with less frequently in other muscles.

The Lungs.—The change in the lungs has been described by Buhl as consisting in swelling of the alveolar epithelium. The epithelial elements are markedly granular from the presence of albuminous and fatty particles, and they become loosened from the alveolar walls. The change affects, more or less, the whole of both lungs. The organs are enlarged, cedematous, and abnormally friable.¹

¹ Buhl, "Lungenentzündung, Tuberkulose, und Schwindsucht."

This change occurs not only in pyrexia, but also in the earlier stages of the process of inflammation. Here also a swollen and granular condition of the protoplasm is met with, especially in epithelial and endothelial elements. It is to this that Virchow gave the name of "cloudy swelling." (See chapter on "Inflammation.")

Respecting the nature of the change—nothing is certainly known. Dr. Wickham Legg produced it artificially in animals by submitting them to a high temperature, and he, in common with some other pathologists, is inclined to look upon it simply as a result of the high temperature. The probability that it is due rather to specific alterations of the blood has been already alluded to. An exact knowledge of its pathology, however, must await further experimental investigation. In the mean time, when it is borne in mind that the conditions in which it occurs are attended by alterations in the blood and in the nutritive processes, and that in advanced degrees of the change it is accompanied by more or less fatty metamorphosis, it may be regarded as probable that its occurrence will be found to be due partly to interference with the normal processes of tissue-oxidation, and partly to increased transformation of the protoplasm of the cells. (See "General Pathology of Fatty Degeneration.")

Whatever be the nature of the change, there can be no doubt that it must very materially interfere with function, and that its occurrence in the course of acute disease, especially when affecting the heart, must constitute a most important source of danger. Although it may lead to more or less fatty degeneration, it tends, if death does not supervene, to terminate in perfect health.

CHAPTER XI.

NUTRITION INCREASED.

THE morbid processes thus far described have been attended either by *arrest* or by *impairment* of nutrition;—those remain to be considered in which the nutritive activity is *increased*. They include the Regenerations, Hypertrophy, and the Tumors.

In considering these results of increased nutritive activity, it must be borne in mind that physiologically the formative power of different tissues varies greatly. During the period of development all the tissues increase, but when this period is completed, their activity is, for the most part, limited to merely maintaining themselves. In some tissues the power of reproduction is completely lost after the natural period of growth is past. Such is the case, for example, with the nervous centres, which when destroyed are never regenerated. In most tissues, however, this formative power is capable under certain conditions of again manifesting itself. There are two important causes of this re-manifestation. One is the destruction or loss of portions of tissue from injury or disease. This, in most structures, causes a formative activity in the cellular elements, and thus leads to the *regeneration* of the lost part.

The other, and most important, cause of a renewal of reproductive activity after the completion of the period of growth is an increased supply of nutritive material. Such increased supply, however, can never lead to new growth in tissues which, like nerve-tissue, are incapable of again exhibiting their reproductive power. The increased supply may be due to simple active or to inflammatory hyperæmia.

Simple active hyperæmia of a tissue, and consequent new growth, is most frequently the result of increased functional activity. Muscular tissue, for example, which does more work, increases in amount. The nervous influence which causes the increased activity of the muscle causes at the same time active hyperæmia, and thus follows new growth. This is seen in the hypertrophy of the muscles of the calf in ballet dancers; also in the hypertrophy of a hollow viscus from obstruction to the exit of its contents—as of the heart from obstruction at the valvular orifices or in the course of the circulation, of the muscular coat of the stomach in stricture of the pylorus, of the intestine above a permanent stricture, and of the bladder in stricture of the urethra. Glandular organs in the same way become hypertrophied when, owing to the loss or incapacity of their fellows, one gland has to do the work of two. This is exemplified by the hypertrophy of one kidney when the other is destroyed by disease. Much less frequently the active hyperæmia which leads to the new growth is due to other causes. The hypertrophy of the spleen in malarial diseases is probably due to an active hyperæmia of the organ caused by the malarial poison; and that of the thyroid gland in Graves' disease, to hyperæmia due to vaso-motor paralysis. (See "Active Hyper-

æmia.”) In all cases the hyperæmia must be of long duration in order to lead to new growth.

The new growth which results from inflammatory hyperæmia will be considered in the chapters on inflammation. Inflammatory growths differ from non-inflammatory ones in being caused by some *injury*, upon the removal of which the process of growth usually ceases. As examples of growths which must be regarded as occupying a kind of border-land between non-inflammatory and inflammatory formations, may be mentioned the development of corns from pressure, and of warts and condylomata from the irritation of unhealthy secretions.

Hypertrophy.

The term “hypertrophy” is only applied to that form of new growth in which all the constituents of an organ are more or less involved, or those constituents, at all events, upon which the peculiar functions of the organ principally depend. An hypertrophied organ is one increased in size and functional power. Hypertrophy, therefore, can rarely result from an inflammatory process, because, as will be seen when speaking of inflammation, this leads mainly to an increase of the connective tissue of organs, and, with this exception, involves only epithelial and endothelial elements. The commonest cause of hypertrophy is, as already stated, that increased nutritive supply which results from increased functional activity. The increased activity is usually induced by a necessity for some increased work; in muscle, for example, in order to overcome some obstruction, in a secreting organ—to secrete more fluid. Such hypertrophies are consequently *conservative* in their nature, and they are often spoken of as *functional* hypertrophies.

The increase in the amount of tissue which constitutes hypertrophy may be owing to an increase in the size, or to an increase in the number, of the histological elements. When it is owing simply to an increase in the *size* of the elements, it is termed *simple* hypertrophy; when to an increase in their *number*, and to the formation of a new tissue, *numerical* hypertrophy, or *hyperplasia*. The two forms of hypertrophy are thus comparable with the two forms of atrophy: in simple hypertrophy as in simple atrophy, there is merely an alteration in the *size*; in numerical—an alteration in the *number* of the elements. In most cases, however, hypertrophy is a hyperplastic

process. In connective tissue and all the connective tissue substances it is invariably numerical; but in muscle and glandular organs there is usually an increase in the size of the elements as well as an increase in their number.

CHAPTER XII.

THE TUMORS.

THE tumors are new formations which in their development and growth are characterized by their *independence* of the rest of the body; they increase in size by virtue of their own inherent activity, which differs from, and is, to a great extent, independent of that of the surrounding tissues. Having attained a certain size, they either remain permanent, or, more frequently, *tend continuously to increase*. Whatever be the nature of the tumor, it is always the direct product of the elements of a pre-existing tissue. In order, therefore, to understand the pathology of these growths, it is necessary to be intimately acquainted with the histology and mode of development of the normal tissues.

ETIOLOGY OF TUMORS.—As tumors are the result of the increased nutritive activity of the elements from which they originate, it will be readily understood that their causes must for the most part be obscure, and that in many cases all that can be said is, that the new growth is the result of the *spontaneous* activity of the elements from which it springs. Sometimes, however, the causes are either wholly or partially ascertainable. They may be divided into *constitutional predisposing*, and *direct exciting*, causes.

Constitutional Predisposing Causes.—That many tumors owe their origin to some constitutional taint, has long been an universally accepted pathological doctrine. The constitutional cause has frequently been regarded as a general one, as consisting either in some alteration in the constitution of the blood, or in some abnormal condition of the physiological processes throughout the entire organism. It was formerly supposed that many new formations were the result of an

exudation from the bloodvessels, and that the elements of the growth were produced spontaneously in the exuded structureless blastema. Such growths were looked upon as the local expression of a vitiated constitution of the blood,—a *dyscrasia*. Although this hypothesis is now universally abandoned, and all new formations are known to originate from pre-existing cellular elements, an alteration in the constitution of the blood or in the performance of the physiological processes throughout the body, is still regarded by many as playing an important part in their causation.

It is the malignant tumors which are thus supposed to owe their origin to the existence of a *general* constitutional taint. These growths are said to be of a *constitutional* origin, in contradistinction to the non-malignant growths, which are looked upon as purely *local*. This hypothesis is principally based upon the clinical characteristics of the malignant growths—their tendency to recur after removal, their multiplicity, and the difficulty or impossibility of completely eradicating them. .

It is said that the development of malignant growths is frequently preceded by an unhealthy state of the constitution—a cachexia. In the majority of cases of malignant formation, however, there is no evidence of any such cachexia preceding the local growth. The individual is usually in good health at the time of the occurrence of the primary tumor. The general impairment of nutrition and emaciation, which constitute the cachexia, are *secondary* to the local growths, and are in direct proportion to their extent and situation:—the more extended the local lesions, the greater the amount of discharge; the more the lymphatics and the digestive organs are involved, the more marked is the attendant cachexia.

The multiplicity of malignant growths is also adduced as an argument in favor of the existence of a general constitutional taint. The fact that malignant growths are frequently multiple, constitutes in itself no ground for such a conclusion. The multiplicity is for the most part a *secondary* phenomenon the secondary tumors resulting from infection by the primary one. Simple *primary* multiplicity is not so characteristic of malignant as of many other tumors—the lipomata, fibromata, and osteomata, are all more often *primarily* multiple than cancer. Multiplicity in many cases is evidence rather of a *local* than of a general taint. Tumors are often multiple in bone, for example, without occurring in other tissues. In such cases there would appear to be a *local* rather than a *general* cause.

The recurrence of the malignant growth after removal at the seat of the operation, may again be owing to the removal having been incomplete, some of the proliferating elements of the growth having been left behind. The cellular elements of malignant tumors often extend into the adjacent tissues for some distance beyond the apparent confines of the tumor, and as the physical characters of the infiltrated tissues differ in no way from those of the healthy, there are no means of certainly determining how far wide of the tumor the incision must be carried in order to include the whole of the affected structures. (See "Malignancy.") A tendency to local recurrence is a property possessed by many growths, and it can be explained on local grounds without the necessity of admitting the existence of a general taint.

Lastly, the fact that malignant growths are usually followed by the development of similar growths in the lymphatic glands and in internal organs may in most cases be more readily explained—as will be seen when speaking of "malignancy"—by regarding these as the result of infection by the primary tumor, than by ascribing them to the existence of a common constitutional cause. The reasons already adduced in a preceding chapter (see "Introduction"), for considering all changes in the constitution of the blood as secondary to local causes, would appear of themselves to be sufficient to render untenable the hypothesis of a *primary* blood dyscrasia. Any abnormal condition of the blood which may be associated with the development of malignant tumors must probably be regarded as resulting either from the absorption of deleterious substances, from the entrance into it of the elements of the growth, from the drain of an attendant discharge, or from interference with the processes of digestion, assimilation, or secretion, or with the formation of the blood itself. At the same time it must be borne in mind, when discussing the possibility of the development of malignant growths being the result of a "blood-disease," that the emigration of white blood-corpuscles may play some part in the process. How far this is the case, as will be seen hereafter, we are at present unable to determine. We know that this emigration constitutes a prominent feature in the process of inflammation, and if future researches should show that it also occurs in the development of malignant new formations whilst in those which are non-malignant it is entirely wanting, it would go far towards rendering the existence of a malignant dyscrasia beyond dispute. In the present position of our knowledge, however, in which it is *only probable* that an emigration of leucocytes may play some part in the develop-

ment of new growths, both innocent and malignant, any argument in favor of the existence of a blood-dyscrasia as the cause of the development of the latter based upon such considerations would be unjustifiable.

Although there would thus appear to be no necessity to admit the existence of a general constitutional cause in order to explain the clinical characters which constitute malignancy, there can be no doubt that the development of many growths, both innocent and malignant, is materially influenced by constitutional conditions. Certain conditions of the constitution may *favor* the development of tumors just in the same way that they favor, for example, the development of syphilitic lesions. In both cases the *local* processes may be modified by the *general* constitutional state. In the case of tumors it must be admitted as possible that the constitutional influence may be sufficient in itself to determine the development of the new growth; and this possibility must be borne in mind in accounting for the development of secondary malignant growths, as although these may result from infection, they may perhaps in some cases owe their origin to the same causes as those which induced the primary one.

The influence of *hereditary predisposition* must also be taken into account in studying the etiology of tumors. This influence is marked in the case of many growths both malignant and benign. The inherited peculiarity is probably, in most cases, a *local* rather than a *general* one, consisting in some constitutional peculiarity of the tissues from which the new growths originate, some peculiarity which renders them more prone than other tissues to undergo abnormal development. In scrofula, for example, which is a markedly hereditary disease, the tendency of the lymphatic glands to undergo excessive development from very slight degrees of irritation, is probably to be regarded as owing to a predisposition of the glands themselves, and not to any *general* constitutional state. The same is probably true of many other constitutional tendencies. *Nævi*, tumors of the skin, uterus, *mammæ*, stomach, and of other parts, are again all unquestionably sometimes hereditary; and here also the tendency would appear to consist in a predisposition of the tissues themselves to become the seats of new formations.

The tendency sometimes observed in *particular* tissues to generate new formations, points again to a local cause. The osseous system, for example, may be the seat of new growths—tumors occurring in

nearly all the bones, and not being met with in other parts. Tumors may in the same way be multiple in other tissues.

Direct Exciting Causes.—The existence of a direct exciting cause is more capable of demonstration than a constitutional one. It consists either in some direct irritation of a tissue, which is by this means stimulated to increased development; or in the migration or transmission of elements from some primary growth, which by proliferating themselves, or causing proliferation, in the tissues in which they lodge, constitute the centres of secondary formations.

The direct irritation of a tissue may be owing to mechanical or chemical irritants. Simple mechanical or chemical irritation can, however, under no circumstances be the *only* cause of the development of a tumor. The effect of such irritations alone, as has been seen in the preceding chapter, is to cause an inflammatory formation, or some of those forms of new growth such as corns, condylomata, and exostoses, which appear to occupy an intermediate position between inflammatory formations and tumors. In order for irritation to cause a tumor, there must be some special predisposition of the tissue itself; the irritation can merely *determine* its development. It does so probably by causing a local hyperæmia and so increasing the supply of nutritive material. The influence of simple irritation in the production of new formations is exemplified by the frequent occurrence of epithelioma on the lips of smokers, from the irritation of the pipe; and on the penis and scrotum of chimney-sweepers, from the irritation of the soot ("chimney-sweeps' cancer"). The numerous recorded instances of the development of a tumor following some external violence or injury, leave little doubt that these also sometimes stand to one another in the relation of cause and effect. Lastly, as pointed out by Virchow, it is those organs which are the most exposed to irritation from external causes, as the stomach, the mammary-gland, and the rectum which are especially liable to become the seats of new growths.

The influence of elements, which have either migrated or been conveyed from their original habitat, in causing the development of new formations is exemplified by the history of malignant tumors. It is by this means that the secondary tumors most frequently originate. The elements, which either migrate spontaneously from the primary growth, or are carried by the blood or lymph streams, may proliferate in the tissue in which they lodge, and so develop into secondary formations.

In other cases it is also exceedingly probable, as pointed out by

Dr. Creighton,¹ that the elements which are transmitted from the primary tumor cause the production of secondary tumors by virtue of an influence on the cells of the tissue where they lodge, which may be termed a *spermatic influence*, and which is comparable with that of the sperm-cell on the ovum. In such cases the relation of the primary to the secondary tumor is that of parent to offspring. This subject will be again alluded to when speaking of "Malignancy."

DEVELOPMENT.—In studying the development of the tumors, it is important, in the first place, to bear in mind what has been already stated—viz., that they are in all cases the direct product of pre-existing cellular elements. Prof. Cohnheim has recently advanced the hypothesis that the cells from which they originate are not those of the mature tissue, but embryonic cells, a few of which not having been utilized in the normal process of development remain over, quiescent for a time, but ready, when from any cause there is increased blood-supply, to renew their formative activity. In support of this view he adduces the facts, that tumors tend to develop and to grow most rapidly when for physiological or other reasons there is any increased supply of blood; and that tumors consisting of a tissue different in type to that of the structure in which they grow (heterologous tumors—*e. g.*, enchondroma of the testicle), are only met with in tissues which are themselves derived from the same primary embryonic layer as is the tissue of which the tumor is composed.² Whether this hypothesis be true or not, it certainly serves to explain some points in the pathology of tumors, and in considering the development and history of these growths it will be well to remember it.

The tumors in their development and structure resemble the normal tissues—every pathological growth has its physiological prototype. The resemblance, however, is by no means complete, for as indicated in the definition, tumors in their development are characterized by their independence of the rest of the organism, so that in this and in their structure they are always more or less *atypical*.

The elements from which tumors most frequently originate are those belonging to the *common connective tissue*, and to the bloodvessels and lymphatic system with which it is so intimately associated. By common connective tissue is meant that tissue which in all parts surrounds the bloodvessels, and is so universally distributed throughout the entire organism. This must be carefully distinguished from the

¹ Discussion on Cancer, *Trans. Path. Soc. Lond.*, 1874, p. 368.

² "Vorlesungen über allgemeinen Pathologie," Band i.

formed connective substances—tendon, cartilage, bone, &c. In this common connective tissue we distinguish two kinds of cells—the stable cells (connective tissue corpuscles), and the mobile cells, which are probably wandering white blood-corpuscles. These cells are in intimate relation with the endothelium of the lymphatics, the latter vessels commencing as serous canals which are universally distributed in the tissue. Further—both the endothelium of the lymphatics and that of the bloodvessels closely resemble in their physiological functions the fixed cells of the connective tissue.

In the process of development of tumors from connective tissue, the part which is played by the different cellular elements cannot in our present state of knowledge be certainly stated. The first result of their activity, however, is to produce a new tissue, composed of small roundish-shaped cells, from $\frac{1}{1800}$ to $\frac{1}{2500}$ of an inch in diameter, inclosing a large ill-defined nucleus. The cells, which possess no limiting membrane but are simply little masses of amoeboid protoplasm,

are inclosed in a scanty, semi-fluid, and faintly granular intercellular material (Fig. 30). This tissue is obviously precisely similar to embryonic tissue. In some cases the protoplasm continues to increase and the nuclei to divide without any subsequent division of the cell taking place, and thus are produced large irregular-shaped masses of protoplasm containing numerous nuclei. These are the giant or myeloid cells which are met with in the medulla of young bone and in many sarcomatous tumors.

(See “Myeloid Sarcoma,” Fig. 51.) Thus the

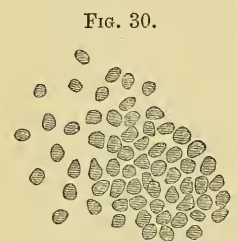


FIG. 30.
*Embryonic (“Indifferent”)
Tissue from the edge of a
Sarcomatous Tumor. X
350.*

first stage in the process of development consists in the formation of an embryonic tissue, and this embryonic tissue subsequently develops into the tissue of which the tumor is composed. It is often impossible to determine in this early stage of the growth what it will ultimately become—whether a fibroma, a sarcoma, or an enchondroma, etc. According to the hypothesis of Cohnheim, the embryonic tissue, as already stated, is not derived from a proliferation of the elements of the mature connective tissue, but from embryonic cells which were not utilized during the period of physiological development.

The second stage of the process consists in the development of this embryonic (“indifferent”) tissue into the tissue of the permanent growth, and this subsequent development closely resembles that of the

immature connective tissue of the embryo. As from the immature connective tissue of the embryo are developed various connective tissue substances—fibrous tissue, mucous tissue, cartilage, bone, etc.—so may this embryonic connective tissue, which constitutes the earliest stage of so many of the pathological new formations, become developed into various tissues, all of which usually more or less resemble the several varieties of the physiological connective tissue. The whole of the primary cells may form the same kind of tissue, in which case the growth will possess the same characters throughout; or it may be complex, some cells forming one kind of tissue and some another. A combination of two or more kinds of structure may thus be met with in the same tumor—as a combination of sarcoma and lipoma, of enchondroma and myxoma, and so on. What determines the ultimate development of the young cells, why they produce such various forms of growths, is as far from our knowledge as what determines the ultimate destination of the cells in the embryo.

Next to connective tissue, the *epithelium* and *glandular structures* are the tissues from which tumors most frequently originate; and as from connective tissue are usually produced growths of the connective tissue type, so do the growths originating from the epithelia usually resemble epithelium. As to whether all new growths originating in connection with epithelium are solely the offspring of pre-existing epithelial elements, we are unable to speak with absolute certainty. The answer to this question must await a more certain knowledge of the way in which the epithelial structures normally grow and repair themselves. It is regarded as probable by some that the normal production of epithelium is not entirely the result of the multiplication of epithelial cells, but that the cells of the connective tissue by *contact* with epithelial elements may become developed into epithelium. If this be so, it must be admitted as at all events equally probable, that pathological new formations which originate in connection with epithelium may be in part the product of elements belonging to the connective tissue. This subject will be again alluded to when speaking of the development of carcinoma. The process of development from epithelium may take place either by simple division, or by vacuolation and endogenous growth.

Here allusion must be made to the recent investigations of Dr. Creighton on the development of secondary tumors in the liver.¹

¹ Discussion on Cancer, *Trans. Path. Soc. Lond.*, 1874, p. 368.

Dr. Creighton finds that in various kinds of secondary tumor occurring in the liver, the growth originates from the liver-cells by a process of vacuolation and endogenous formation; and he concludes that in this way liver-cells may originate epithelial cells, connective tissue-cells, spindle-cells, etc., the variations depending upon the nature of the primary tumor.

From the remaining tissues, *muscle* and *nerve*, the development of tumors is comparatively rare, and in the highest nerve-tissue it is doubtful if formative processes ever occur.

According to the similarity or difference which subsists between the new growth and the tissue from which it grows, tumors are divisible into two classes—*homologous* and *heterologous*. When the tumor resembles in its structure and development the tissue from which it originates, it is said to be homologous; when it differs, it is said to be heterologous. A cartilaginous tumor, for example, growing from cartilage, is homologous, but growing from any other tissue, as from the parotid gland, it is heterologous. The same variety of tumor may thus be in one case homologous, in another heterologous. Heterology, however, is not limited to the production of a tissue which is dissimilar from that from which it originates; a tumor is also said to be heterologous when it differs from the tissue in which it is *situated*, and this may occur without its being the direct product of the latter. It is heterology in this sense that is so characteristic of malignant growths. Cancers, for example, become heterologous owing to the growth and extension of the epithelium beyond its normal limits (see "Epithelioma," Fig. 61); and the same form of heterology obtains in the case of growths originating from elements which have migrated or been carried from their original habitat, and have developed into a tissue which differs from that in which they are situated.

RELATION OF THE TUMOR TO THE SURROUNDING TISSUES.—The relation of the tumor to the surrounding structures will depend upon its mode of growth. This may be circumscribed or diffuse. In the former case the tumor will merely displace the surrounding parts, and having attained a certain degree of development, a fibrous capsule is often formed around it, by which it becomes completely isolated. The lipomata, fibromata, and enchondromata are usually thus encapsuled. In other cases the growth is diffuse and invades the adjacent structures. There is then no line of demarcation between the tumor and the surrounding parts, so that, although to the naked eye it

may appear separate, the microscope will discover in the adjacent tissues elements of the new growth. (Fig. 31.) This is characteristic of malignant tumors, and is a common cause of local recurrence after removal. (See "Malignancy.")

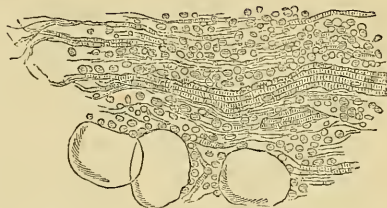
RETROGRESSIVE CHANGES.—A tumor never actually disappears, and it thus differs from an inflammatory growth—for example, from a syphilitic gumma. It may remain stationary, or grow slowly or rapidly, and sooner or later it usually becomes the seat of retrogressive changes. The time

at which these commence varies: As a rule the permanence and durability of a tumor bear an inverse relation to the rapidity of its growth, and to the inferiority of its organization. The more rapid the growth, and the more lowly organized the tissue formed, the less its durability and the sooner do retrogressive changes occur. The carcinomata and sarcomata, for example, which develop rapidly, and consist for the most part of cells, quickly degenerate; their elements are unstable and soon perish. Osseous tumors, on the other hand, which develop more slowly, and consist of a more highly organized tissue, have a much greater stability, and are but little liable to retrogressive metamorphosis.

The retrogressive changes are similar to those met with in the physiological tissues. Deficient supply of blood is followed by fatty degeneration and its various terminations—softening, caseation, and calcification. Pigmentary, colloid, and mucoid degeneration may also occur. Tumors may also become the seats of an inflammatory process, of ulceration, hemorrhage, and necrosis.

MALIGNANCY.—By "malignancy" is understood the property possessed by many tumors of reproducing themselves either locally after removal, or in distant tissues. It is important not to confound the terms "malignancy" and "cancerous." "*Malignancy*" is a purely clinical term, and although in a high degree the property of the carcinomata, is by no means confined to them; the sarcomata, for example, being in many cases equally, or even more malignant. The

FIG. 31.



Scirrhus of the Mamma.—A thin section from the most external portion of the tumor. Showing the invasion by small-celled infiltration of the muscular fibres and adipose tissue in the neighborhood of the gland. $\times 200$.

term "*cancerous*," on the other hand, is used to imply a definite structure, and as such is applied to a certain class of new formations.

The malignant properties of a tumor may manifest themselves either in the tissues immediately adjacent to it or in its neighborhood, in the nearest chain of lymphatic glands, or in more distant parts. Some growths possess these properties in a higher degree than others, so that there are different degrees of malignancy. In many cases the malignancy of a tumor is so far limited that it gives rise merely to a local reproduction after removal. Such tumors have been separately classified by many surgeons as "recurrent" tumors. (See "Small Spindle-celled Sarcoma.") In other growths this tendency to local reproduction is associated with the development of similar growths in the nearest lymphatic glands; whilst in a third class of cases, to one or both of these conditions is added the reproduction of the growth in more distant tissues, especially in the lungs and liver. It will be advisable to treat of these three degrees of malignancy separately.

1. *Reproduction of the Tumor in the Adjacent Structures.*—This is usually the earliest evidence of malignancy in a growth, and gives rise to its persistent recurrence *in loco* after removal by the surgeon. This tendency to the local reproduction of the tumor is principally owing to its mode of growth. The cellular elements of the tumor invade the adjacent structures, and often extend for some distance into them, so that unless in the operation for its removal the incision be carried for some distance beyond the *apparent* confines of the growth, some of the elements may be left behind and thus constitute the centres of secondary formations. (See Fig. 31.) The elements of malignant tumors may probably also, as already stated, induce by the influence of *contact* similar developmental changes in the cells of the surrounding tissue. It is this influence which, according to Professor Maier, Dr. Creighton, and other pathologists, is especially characteristic of the cancers, and gives to these tumors their peculiar infective properties. The epithelial growth is not at first infective, but when its development has reached a certain height it exercises an infective influence upon the cells of the neighboring connective tissue and causes them in their proliferation to assume an epithelial type.¹ (See "Development of Carcinoma.") Malignant tumors are not

¹ See Paper by Dr. Creighton "On the Infection of the Connective Tissue in Scirrhus Cancers of the Breast." *Journal of Anatomy and Physiology*, vol. xiv.

usually encapsuled, but in some cases tumors which possess a distinct capsule infiltrate the surrounding structures. The infiltration of the adjacent tissues by the elements of the tumor sometimes gives rise, not only to the continuous enlargement of the primary growth, but also to the development of separate secondary growths in the immediate vicinity of the primary one.

2. *Reproduction of the Tumor in the nearest Lymphatic Glands.*—This is owing to the transmission by the lymph-stream of cellular elements derived from the malignant growth, which become arrested in the nearest lymphatic glands, and there cause the development of secondary formations. These are in all cases of the same nature as the primary tumor. When the lymphatic glands have themselves developed into secondary growths, they in their turn constitute new centres of infection, and may thus infect more distant glands or the immediately adjacent tissues. The tendency to reproduction in the lymphatic glands varies very much in the different varieties of malignant growths, being, for example, very marked in the carcinomata, whereas in the sarcomata it is less frequent. The reasons for these differences will be seen in the subsequent chapters.

3. *Reproduction of the Tumor in Distant Tissues.*—This is usually the terminal process in the history of malignant growths. The reproduction of the malignant growth in distant tissues is in the great majority of cases owing to the entry of some of its elements into the blood-stream. The secondary tumors, as in the lymphatic glands, are in all cases of the same nature as the primary one, although they are often softer, more vascular, and show greater activity of growth. They occur as a rule in those organs through which the blood from the primary tumor first passes—that is in those organs which present the first set of capillaries for the arrest of the transmitted materials. In malignant diseases of those organs, for example, which return their blood through the portal vein, as the stomach and mesenteric glands, it is the liver in which the secondary growths usually first occur, and when this has become involved, it may constitute a secondary centre of affection, and in the same way cause tertiary growths in the lungs. Although this sequence is the rule, there are numerous exceptions. In some cases, the organs which are nearest in the course of the circulation to the primary growth escape, whilst those more distant become affected. This may be owing to one organ being more favorable to the development of the transmitted elements than another; or to the capillaries of the proximal organ allowing elements to pass

through them, whereas those of the more distant one are small enough to arrest them. Lastly, it must be borne in mind that the secondary growths may be entirely independent of the primary one, their origin being due to the same cause.

Although the general dissemination of a malignant growth is thus in most cases owing to the transmission of its elements by the blood-stream, this is not the only way in which it may be brought about. Exceptional cases have been described in which the elements of a tumor have been distributed and caused secondary growths in other ways—as by passing down the trachea, travelling between the layers of the peritoneum, and from the kidneys down the ureters to the bladder, etc.

The secondary tumors, as already stated, are probably either the direct products of the transmitted elements which proliferate in the tissues in which they lodge, or they owe their origin to the infective influence of those elements upon cells with which they come into contact.

It is thus obvious that the evidences of malignancy in a tumor will consist—in its invasion of the surrounding structures, the implication of the neighboring lymphatics, and the occurrence of similar tumors in internal organs. As a general rule it may be stated that the more juice a growth contains, and the richer it is in bloodvessels and lymphatics, the more quickly will it infect the lymphatic glands, and internal organs; on the other hand, the poorer it is in bloodvessels and lymphatics, the more are its infecting properties confined to the neighboring tissues.

The determination of the innocent or malignant nature of any growth will principally depend upon its microscopical characters, and, as will be seen when considering the various kinds of tumors, the differences which exist in their clinical characters are in great measure to be explained by differences in their position, minute structure, and mode of growth. Many varieties of tumors are invariably malignant, as the carcinomata and sarcomata; hence any growth which from its minute structure must be included under these heads, must be regarded as being of a malignant nature.

CLASSIFICATION.—Tumors may be classified upon a histological, or upon a physiological and clinical basis. Although a physiological and clinical classification is much to be desired, in the present state of our knowledge, they must be very incomplete. The usual classification of tumors according to their histological characters is consequently

here adopted. Such a classification may be most advantageously made in accordance with the classification of the physiological tissues:—

Classification of Tumors.

I. *Type of the Fully Developed Connective Tissues.*

Type of fibrous tissue . . .	Fibroma.
“ adipose tissue . . .	Lipoma.
“ cartilage . . .	Enchondroma.
“ bone . . .	Osteoma.
“ mucous tissue . . .	Myxoma.
“ lymphatic tissue . . .	The Lymphomata { Hodgkin's Disease. Leukæmia.

II. *Type of Higher Tissues.*

Type of muscle . . .	Myoma.
“ nerve . . .	Neuroma.
“ bloodvessels . . .	Angioma.
“ papillæ of skin or mucous membrane . . .	} Papilloma.
“ secreting glands . . .	
	Adenoma.

III. *Type of Embryonic Connective Tissue.*

The Sarcomata.

Spindle-celled sarcoma . . .	{	Small-spindle-celled sarcoma.
		Large “ “
		Melanotic sarcoma.
		Osteoid sarcoma.
Round-celled sarcoma . . .	{	Glioma.
		Alveolar sarcoma.

IV. *The Carcinomata.*

Scirrhus.
 Encephaloid.
 Colloid.
 Epithelioma—Adenoid Cancer.

V. *Cystic Tumors.*

Cysts.

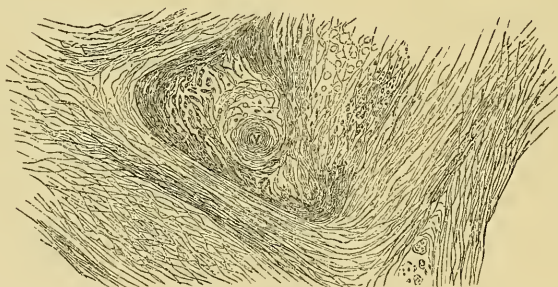
CHAPTER XIII.

THE FIBROMATA.

THE fibromata, fibrous, fibro-cellular, or connective-tissue tumors, are tumors consisting of fibrous tissue.

STRUCTURE.—In structure the fibromata present the same variations as those met with in fibrous tissue. Some of them are composed of firm, dense, fibrous tissue, such as constitutes tendons; others are laxer and less fibrous in consistence, more resembling the connective tissue of the cutis. The fibres, which constitute the chief part of the growth, are more or less closely interlaced, and are distributed without any definite arrangement, or grouped in bundles of various sizes. They are sometimes arranged concentrically around the bloodvessels. (Fig. 32.) Yellow elastic fibres are but very rarely met with. The

FIG. 32.



Section of a Fibrous Tumor from the Skin.—In the neighborhood of the cut bloodvessel *v*, are seen some cells; also fibres cut transversely. $\times 200$ and reduced $\frac{1}{2}$.

cells, like those of normal fibrous tissue, are very few in number, and are usually most abundant around the vessels. They are minute, spindle-shaped, fusiform, or stellate bodies, the latter having processes of varying length, which communicate with similar processes from neighboring cells. They are often so small and indistinct as in the fresh specimen only to become visible after the addition of dilute acetic acid. The size and number of these cells vary with the rapidity

of growth—the slower the growth the more fibrous the tissue, and the smaller and less numerous are the cells.

The fibromata usually contain but few bloodvessels. In the softer growths, however, these are often more numerous. They sometimes form a cavernous network, the walls of which are firmly united to the tissue of the tumor, so that when divided or ruptured they are unable to retract. In such cases, injury to the tumor is often followed by profuse hemorrhage.

DEVELOPMENT.—The fibromata originate from connective tissue, either from the cutis or subcutaneous connective tissue, from the submucous or subserous tissue, from fasciæ, the periosteum, the neurilemma, or from the connective tissue of organs. In the earliest stages of their growth the cells are more numerous than when development is complete. (See “Development of Tumors.”)

SECONDARY CHANGES.—Of these, partial mucoid softening and calcification are the most common. Ulceration also sometimes occurs in those growths which are situated in the skin and submucous tissue.

VARIETIES.—Fibrous tumors present some variations in their characters, which depend for the most part upon the tissue from which they grow. Two classes may be distinguished:—

1. *Soft Fibromata*.—These consist of the looser and less dense form of fibrous tissue. They are met with as diffused growths in the subcutaneous and submucous tissue. In the former situation they often form large pedunculated and non-encapsuled tumors, which are commonly known as *wens*. These are sometimes multiple. A similar increased growth of the subcutaneous tissue is also met with in *Molluscum Fibrosum*. In this disease the large masses which hang down from the thighs, buttocks, and other situations consist simply of loose fibrous tissue. The new growth here often contains numerous large bloodvessels, so that its removal may lead to dangerous hemorrhage.

In addition to these diffused growths, more circumscribed and *encapsuled* fibrous tumors of the soft variety are occasionally met with growing from the scalp, scrotum, labium, intermuscular septa, and other situations.

2. *Firm Fibromata*.—These are composed of dense fibrous tissue resembling that met with in tendons. They are firm, hard, encapsuled tumors, presenting on section a grayish-white, glistening, fibrous appearance. These tumors often occur in connection with bone, especially with the upper and lower jaws, originating either in the centre of the bone or from the periosteum. Growing from the periosteum of the

alveolus they constitute simple fibrous *epulis*. They are also met with in the nose, where they form one variety of *nasal polypus*. It is in these firm fibrous growths that the communication of the blood-vessels with cavernous spaces already alluded to, is sometimes found.

Another variety of firm fibrous tumor grows in connection with nerves, and is often described as *neuroma*. True neuromata, however, —*i. e.* new formations of nerve-tissue—are amongst the rarest forms of new formations. These fibrous growths most frequently occur in connection with the superficial nerves. They grow from the neurilemma, and as they increase in size the nerve-fibres become expanded over them. They are very firm, rounded tumors, and are frequently multiple.

The fibroid tumors of the uterus, which are often described as fibrous tumors, are in most cases over-growths of the involuntary muscular tissue of the organ. They will therefore be considered with the muscular tumors. (See “Myoma.”)

CLINICAL CHARACTERS.—Clinically the fibromata are perfectly innocent. They grow slowly, and have no tendency to recur locally after removal.

Psammoma.

This is perhaps the best place to allude to a rare form of growth occasionally met with in the brain and its membranes, which is known as psammoma. The most characteristic feature of this growth is that it consists largely of calcareous particles. These are contained in the concentric bodies already described as the corpora amylacea, where they give rise to the so-called “brain-sand”:—hence the name of the growth. The calcified corpora amylacea, associated with a varying quantity of a cellular and fibrillated tissue, and bloodvessels, make up the growth.

Psammoma is usually met with growing from the membranes of the brain, or from the choroid plexus. In the latter situation it often contains numerous cysts. It is of no pathological importance except when of sufficiently large size to produce symptoms from pressure.

CHAPTER XIV.

THE LIPOMATA.

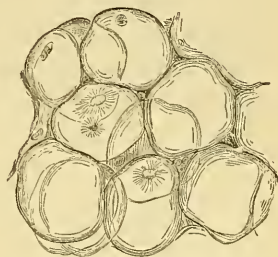
A GENERAL new formation of adipose tissue, constituting *obesity*, has already been described under "fatty infiltration." A localized and circumscribed formation constitutes a *lipoma* or fatty tumor.

STRUCTURE.—The lipomata resemble in their structure adipose tissue. (Fig. 33.) They consist of cells containing fat, and a variable quantity of common connective tissue. The cells, like those of adipose tissue, though usually somewhat larger, are more or less round or polygonal in shape, and are distended with fluid fat. The nucleus and protoplasm are so compressed against the cell-wall by the fluid contents, that, although their existence may often be demonstrated by treatment with reagents, they are usually only readily visible when the cell is atrophied and contains less fat. (See Fig. 4 a.) The connective tissue, which varies in amount, usually unites the cells in masses or lobules of various sizes, and also in most cases forms a thin capsule around the tumor. Bloodvessels are distributed in the fibrous septa.

DEVELOPMENT.—The lipomata grow from connective tissue. Adipose tissue, it must be remembered, is merely connective tissue containing numerous cells which are infiltrated with fat; and its growth consists, either in the infiltration of more of these cells, or in a proliferation of the cells, and an accumulation of fat in those newly developed. A lipoma in the same way originates by a localized proliferation of cells, which as they are produced become infiltrated with fat. The growth of these tumors is always very slow, and they are usually encapsuled by a layer of fibrous tissue.

SECONDARY CHANGES.—Secondary changes in the lipomata are not common; their fibrous septa may, however, become calcified, or even ossified, and the fatty tissue undergo a process of liquefaction. Soft

FIG. 33.



Lipoma. Some of the cells contain crystallized fatty acids. $\times 200$.

ening may also occur from a mucoid change. Inflammation of these tumors is rare, but when situated in the subcutaneous tissue the skin over them may become adherent and ulcerate.

PHYSICAL CHARACTERS, ETC.—The situation of the lipomata is almost co-extensive with that of adipose and connective tissue. They occur most frequently, however, in those parts in which fat is normally met with, as in the subcutaneous tissue and the inter-muscular septa. They are also occasionally developed in the subsynovial and subserous tissues, in the submucous tissue of the stomach and intestines, and even in internal organs. They sometimes attain an enormous size. They are more or less lobulated, and are usually surrounded by a fibrous capsule which separates them from the adjacent structures. On section they present the ordinary appearance of adipose tissue. Their consistence varies with the amount of fibrous tissue which they contain. They are usually single, although not unfrequently multiple. In their growth they occasionally become pedunculated.

CLINICAL CHARACTERS.—Clinically, the lipomata are perfectly innocent.

CHAPTER XV.

THE ENCHONDROMATA.

THE Enchondromata are tumors histologically resembling cartilage.

STRUCTURE.—Like cartilage they consist of cells and an intercellular substance, which present all the variations observed in the normal tissue. The intercellular substance may be hyaline, faintly or distinctly fibrous, or mucoid. When fibrous, the fibres may be arranged like those of fibro-cartilage, or more or less concentrically around the cells, as in the reticular cartilages of the ear and larynx. (Fig. 34.) When hyaline or mucoid, it is sometimes quite soft in consistence. The cells may be very numerous, or few in proportion to the matrix. They are round or oval, and occasionally branched and stellate. In the hyaline

FIG. 34.



Fibrous Enchondroma.
X 200.

forms they are usually large and round or oval (Fig. 35); in the fibrous forms they are often smaller and even somewhat spindle-shaped, more resembling those of connective tissue; and in the rarer mucoid forms, they are more commonly stellate and branched, like those of the umbilical cord. They are either single or arranged in groups, and are usually surrounded by a capsule, as in normal cartilage, although this is often very indistinct. They inclose one or more nuclei and slightly granular contents; sometimes a cell-wall cannot be distinguished. In addition to the intercellular substance, the growth is usually divided into several lobes by bands of fibrous tissue, in which are contained the bloodvessels. These lobes are often very distinct, so that the growth appears to be made up of several separate tumors. The fibrous tissue in most cases also encapsules the growth, and separates it from the surrounding structures, although sometimes this encapsulation is absent, and the tumor is surrounded by a zone of embryonic cells, which infiltrate the adjacent tissues.

FIG. 35.

*Hyaline Enchondroma.* $\times 200$.

DEVELOPMENT.—The enchondromata most frequently originate from bone and common connective tissue, very rarely from cartilage. Cartilage itself, and especially fibrous cartilage, is very closely allied to common connective tissue. It grows from the deeper layers of the perichondrium, which proliferate and form an embryonic tissue; the young cells become cartilage cells, and these probably form the matrix, which is either homogeneous or fibrillated, constituting in the one case hyaline, and in the other fibrous cartilage. The development of enchondroma from connective tissue is precisely similar to the physiological progress.

In the development of enchondroma from osseous tissue the medulla is the source of the new growth. This proliferates, the osseous trabeculae are absorbed, the neighboring medullary spaces open one into the other, and in this manner a large medullary cavity is produced. In the centre of this the young cells first formed enlarge and become separated by a homogeneous, or, less frequently, slightly fibrillated intercellular substance, and thus is produced a mass of cartilage in the centre of the medullary tissue. This gradually increases till ultimately a layer of fibrous tissue is formed around it, and its further growth takes place from the tissue of its capsule.

Lastly, cartilaginous growths may originate from cartilage itself. These are sometimes seen on the surface of the articular cartilages, in the larynx and trachea, and on the costal and intervertebral cartilages. They are simply local overgrowths from pre-existing cartilage. They rarely attain a large size, and in structure and physical characters more closely resemble normal cartilage than the other forms of enchondroma. They are usually described as *enchondroses*, and must be distinguished from the other forms of cartilaginous tumor.

SECONDARY CHANGES.—Of these, calcification is much the most common. It affects different parts of the growth, commencing in the capsules, and then involving the intercellular substance. Ossification also occasionally occurs; it commences at separate centres, and spiculæ of bone are formed which traverse the tumor in various directions. Fatty degeneration and mucoid softening are common changes, and may lead to the formation of large softened masses which present the appearance of cysts. In rare cases the skin covering the tumor ulcerates, and a fungating mass protrudes.

VARIETIES.—The varieties of enchondroma depend mainly upon the nature of the intercellular substance. There are thus hyaline, fibrous, and mucoid enchondromata; these, however, are usually combined in various degrees in the same tumor. As a rule, those originating from the medulla of bone are of the hyaline and mucoid class, whilst those originating from connective tissue in other situations are more frequently fibrous. The rapidly-growing fibrous forms approach very closely the confines of the sarcomata; the mucoid forms the confines of the myxomata; and these two kinds of growth are often associated in the same tumor.

A variety of enchondroma has been described under the name of *osteo-chondroma*, which in structure more closely resembles bone than cartilage. It consists of a tissue similar to that met with between the periosteum and bone in rickets, which from its resemblance to osseous has been called *osteoid*, tissue. This tissue only requires calcifying to become true bone. Like bone it is made up of trabeculæ and medullary spaces, but the trabeculæ, instead of bone-corpuscles and lamellæ, consist of small angular cells without a capsule, situated in an obscurely fibrillated matrix, which in part is calcified. The medullary spaces contain a fibrous stroma and many bloodvessels. The osteo-chondromata, although consisting mainly of this osteoid tissue, contain also a small proportion of cartilage. They originate beneath the periosteum, their common seat being the ends of the long bones.

Their growth is very rapid, and they often attain an enormous size. They are much more freely supplied with bloodvessels than the ordinary enchondromata, and hence they are much less frequently the seats of retrogressive changes. They are especially prone to become ossified and converted into true bone.

PHYSICAL CHARACTERS, ETC.—The enchondromata occur most frequently in early life. About three fourths of them are met with in the osseous system, where they grow either from the medulla or from the periosteum. Their favorite seat is the fingers and toes. The remaining fourth occur most frequently in the parotid gland and in the testicle. They occasionally occur in the inter-muscular septa, in the subcutaneous cellular tissue of the mamma, and in the lungs. They are usually single, except when occurring on the fingers and toes, in which situations they are more frequently multiple. They consist of a single tumor, or of several smaller tumors held together by fibrous tissue. The more slowly growing enchondromata are hard, smooth, elastic tumors, often lobulated, and seldom exceeding the size of an orange. Less frequently these tumors grow very rapidly, are quite soft in consistence, and attain a large size.

CLINICAL CHARACTERS.—The enchondromata must for the most part be regarded as innocent growths. They are usually encapsuled, and in most cases produce merely local effects, although these, from the parts involved and the rapidity of the growth, are often very injurious. The softer forms, however, and especially those which occur in the medulla of bone and in the glands, occasionally exhibit malignant characters. These grow the most rapidly, and are often not limited by a fibrous capsule, but surrounded by a zone of embryonic tissue. Such tumors tend to recur locally after removal, and in rare cases also infect the lymphatic glands, and are reproduced in the lungs. In speaking of the malignancy of these enchondromata, it must be borne in mind that they are sometimes associated with sarcoma, and the malignant properties are probably in all cases to be ascribed to the combination of sarcomatous with the cartilaginous elements.

CHAPTER XVI.

THE OSTEOMATA.

THE Osteomata, or osseous tumors, are tumors consisting of osseous tissue. A new formation of bone occurs under various circumstances. Irritative conditions of the bone and periosteum are often attended by a large formation of new bone. This is seen after fractures, in which there is not only a formation of bone from the bone itself, but also from the periosteum and adjacent fibrous structures ("permanent" and "provisional callus"). Chronic inflammation of the periosteum is also frequently followed by thickening of the bone beneath it. These, however, are inflammatory formations, and have not an independent growth like the osseous tumors.

STRUCTURE.—Osseous tumors resemble in structure normal bone. There are three histological varieties:—

1. *The Eburnated Osteomata*.—These consist of dense, compact, osseous tissue. The lamellæ are arranged concentrically and parallel to the surface of the tumor. There is a complete absence both of bloodvessels and of cancellous tissue.

2. *The Compact Osteomata*.—These are formed of a tissue similar to that of the compact tissue of the long bones; differing only in the arrangement of the Haversian canals and canaliculi, which is less regular than in normal bone.

3. *The Cancellous Osteomata*.—These consist of cancellous osseous tissue, which is usually surrounded by a thin layer of denser bone. The medullary spaces may contain embryonic tissue, a fibrillated tissue, or fat.

DEVELOPMENT.—Osseous tumors originate from bone or its periosteum, from cartilage, and from connective tissue apart from bone.

VARIETIES.—The osteomata are divisible into two classes, according to their seat—the homologous osteomata or *exostoses*, and the heterologous osteomata or *osteophytes*.

The *homologous osteomata* or *exostoses*, are outgrowths from pre-existing bone, growing either from the periosteum, from the articular cartilage, or from the medulla. Those growing from the periosteum

occur most frequently on the external and internal surfaces of the skull: the orbit is an especially favorite seat, and here they are often dense and eburnated. They are also met with on the scapula, pelvis, and on the upper and lower jaws. In the last-named situation they may grow from the dental periosteum. There is usually a line of demarcation between them and the subjacent bone, the new tissue of the tumor being distinct from the compact tissue of the bone. The periosteum from which they grow covers them, and is continuous with that of the old bone.

The exostoses growing from the articular cartilages occur at the ends of the long bones. In structure they are much more cancellous than the periosteal growth, and their outline is less regular. The medullary exostoses—or more properly, *enostoses*—are the least frequent: they originate in the medullary tissue.

The *heterologous osteomata* or *osteophytes*, originate apart from bone, growing from connective tissue. They are especially liable to occur in tissue in the neighborhood of bones which are the seat of a chronic inflammatory process, and they must in most cases be regarded rather as inflammatory formations than as tumors. Such formations of bone are sometimes met with in the neighborhood of diseased joints and of diseased bone in other situations, in tendons, in the cartilages of the larynx in chronic laryngitis, in the costal cartilages, in the bronchi, in muscle, in the arachnoid and pia mater, and even very occasionally in the lungs and brain. They must be distinguished from calcareous deposits, in which there is no new formation. (See “Calcareous Degeneration.”)

CLINICAL CHARACTERS.—The osteomata are perfectly innocent tumors. Their growth is very slow. They rarely attain a large size. They are often hereditary and multiple, in which case they usually occur in early life. Those osseous growths which sometimes exhibit malignant characters, are enchondromata or sarcomata which have undergone partial ossification. From these, true osteomata must be carefully distinguished. (See “Osteoid Sarcoma.”)

CHAPTER XVII.

THE MYXOMATA.

THE Myxomata are tumors consisting of mucous tissue. Mucous tissue is a translucent and succulent connective tissue, the intercellular substance of which yields mucin. Physiologically, this tissue is met with in two forms, and in two situations: one—in the vitreous body of the eye, in which the cells are roundish and isolated; the other—in the umbilical cord, in which the cells are fusiform or stellate, and give off fine prolongations which anastomose with one another. In both, the intercellular substance is homogeneous and yields mucin. The connective tissues in their embryonic condition, as already stated when describing “muroid degeneration,” possess an intercellular substance containing large quantities of mucin. This is especially the case with the tissue which subsequently becomes adipose. New formations may undergo a muroid change, and thus closely resemble in their physical and chemical characters the myxomata. A myxoma, however, is a

growth which consists of mucous tissue. The myxomata are thus very closely allied to the sarcomata, and by many are included in the same class of new formations.

STRUCTURE.—The cells present the two varieties met with in the physiological tissues. The majority are angular and stellate, with long anastomosing prolongations. (Fig. 36.) Others are isolated, and fusiform, oval, or spherical in shape. They usually possess one, in some cases two distinct nuclei. Their contour is very indistinct, owing to the refracting nature of the intercellular substance. The

FIG. 36.



Myxoma.—A minute piece of a myxoma of the arm, showing the characteristic branched anastomosing cells. There are also a few leucocytes, and one or two spindle-shaped elements. $\times 200$.

latter is very abundant, perfectly homogeneous, of a soft gelatiniform viscid consistence, and yields large quantities of mucin: amongst it

are a varying number of amœboid cells. The bloodvessels, which are not numerous, are readily visible and easily isolated. A few elastic fibres are sometimes seen between the cells.

DEVELOPMENT.—The myxomata always originate from one of the connective tissues. Adipose tissue is their most favorite seat—either the subcutaneous, the submucous, or the intermuscular adipose tissue. They also grow from the medullary tissue of bone, the connective tissue of organs, from the connective tissue of the brain and spinal cord, and from the sheaths of nerves. They are usually separated from the surrounding structures by a very thin fibrous capsule, fine prolongations from which divide the growth into lobules of various sizes. In exceptional cases they may increase by the continuous invasion of their matrix. Their growth is usually slow, but they may attain an enormous size.

SECONDARY CHANGES.—Of these the most common is rupture of the capillaries, hemorrhage, and the formation of sanguineous cysts; this, however, is less frequent than in the sarcomata. The cells themselves may undergo mucoid or fatty degeneration, and thus be destroyed: this is usually accompanied by liquefaction of the intercellular substance.

VARIETIES.—The varieties of myxoma depend principally upon its combination with other growths. The most common is a combination with lipoma. Combinations with sarcoma, enchondroma, and adenoma, are also met with.

PHYSICAL CHARACTERS, ETC.—The myxomata are of a peculiar soft gelatiniform consistence, and of a pale grayish or reddish-white color. Their cut surface yields a tenacious mucilaginous liquid, in which may be seen the cellular elements of the growth. They are most frequently met with in the later periods of life. Growing from the sheaths of nerves, they constitute one variety of so-called neuroma. They may also grow from the placenta, constituting the “uterine hydatids.” When situated in superficial parts they may become pedunculated. In the submucous tissue of the nose they constitute one form of nasal polypus.

CLINICAL CHARACTERS.—Clinically the myxomata are for the most part benign growths. If completely removed they rarely recur. Sometimes, however, they exhibit malignant characters, and recur locally after removal. They probably never reproduce themselves in internal organs. In speaking of their malignancy their occasional association with sarcoma must be borne in mind.

CHAPTER XVIII.

THE LYMPHOMATA.

THE Lymphomata are new formations consisting of lymphatic, or as it is sometimes called, adenoid tissue (the "adenoid tissue" of His). Lymphatic tissue is the tissue composing the follicles of the lymphatic glands and the Malpighian corpuscles of the spleen, and existing in many other parts belonging to the lymphatic system. This tissue is now known to have a much more general distribution than was formerly supposed; it not only constitutes the follicles of the lymphatic glands and the Malpighian corpuscles of the spleen, but also Peyer's glands and the solitary glands of the intestines, the follicles of the pharynx and tonsils, the thymus gland, and the trachoma glands of the conjunctiva. Recently it has also been found to exist in many other situations, as around the bloodvessels of the pia mater and of other parts, in the neighborhood of the smallest bronchi, in the pleura immediately beneath its endothelium, in the peritoneum, in the mucous membrane of the alimentary canal, and in the medulla of bone.

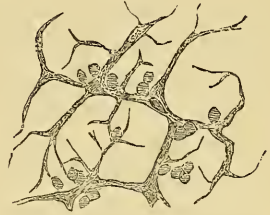
STRUCTURE.—Lymphatic tissue, wherever it exists, possesses the same general structure, and the follicle of a lymphatic gland may be taken as the type not only of the physiological tissue but also of the pathological growths.

This tissue consists essentially of a delicate reticulum, within the meshes of which are contained numerous lymphatic elements—the so-called lymph-corpuscles. The reticulum is made up of very fine fibrils which form a close network, the meshes of which are only sufficiently large to inclose a few, or even a single corpuscle, in each. The fibrils usually present a more or less homogeneous appearance, and nuclei are sometimes to be distinguished at the angles of the network. (Fig. 37.) The lymphatic cells, or lymph-corpuscles, which constitute the greater part of the tissue, can in most cases be readily removed from the meshes of the reticulum by the agitation of thin sections in water. They are identical in their characters with the white cells of the blood. As usually seen after death, they are

spheroidal, pale, semi-transparent bodies, varying considerably in size, and also presenting slight differences in their structure. Some are granular, and appear to possess no nucleus; in others, a distinct, simple, or compound nucleus is visible, which is usually also granular; others again are much larger, and contain two or even three nuclei. (Fig. 38.)

The histological characters of the lymphomata, however, vary considerably, according to the rapidity of their development. In the rapidly growing forms the proportion of cells is very great, and many of these are larger than those normally met with in lymphatic glands, containing two, or even more, nuclei. The more slowly growing tumors, on the other hand, are less richly cellular, and the reticulum constitutes a more prominent part of the growth. (Fig. 39.) In these the larger cell-forms also are almost entirely wanting; and the reticulum, instead of being exceedingly delicate, is much coarser, and forms

FIG. 37.



Lymphoma.—A thin section of a lymphomatous tumor of the mediastinum, from which most of the cells have been removed by penciling. Showing the reticulated network, and the nuclei in its angles. This network is much coarser than that usually met with. $\times 200$.

FIG. 38.



Cells from a Lymphatic Growth in the Liver.—Those to the left are the ordinary lymph-corpuscles which constituted the greater part of the growth. To the right are some of the larger elements. $\times 350$.

FIG. 39.



Lymphoma.—Section of a firm lymphoma of the mediastinum. Showing a very thickened reticulum, within the meshes of which the lymphoid cells are grouped. $\times 200$.

a network of broad homogeneous or slightly fibrillated bands. As the reticulum increases the lymph corpuscles gradually diminish in number and become arranged in smaller groups within its meshes. (See Fig. 39.) These variations in the proportion of cells and stroma are precisely analogous to those met with in lymphatic glands

as the result of acute and chronic inflammation. (See "Inflammation of Lymphatic Structures.")

DEVELOPMENT.—The lymphomata originate for the most part from lymphatic tissue, being simply overgrowths of pre-existing lymphatic structures—mainly of the lymphatic glands. They are, therefore, usually homologous. They may, however, be heterologous, either owing to the new tissue extending considerably beyond the confines of the old, or to its growth in situations, where it is normally almost entirely wanting. This latter condition obtains in Hodgkin's disease, and in certain forms of lymphoma which are malignant.

In considering the development of these growths it must be borne in mind that enlargements of lymphatic structures are most frequently of an inflammatory nature, being due to some injury; and histologically, as already indicated, there is but little difference between these inflammatory growths and lymphomatous tumors. The inflammatory growths, however, tend to subside, the tumors continuously to increase. Further, the development of the tumors may, like that of the inflammatory growths, be determined by some injury, the injury producing perhaps some inflammation and enlargement of the gland, but this instead of subsiding continues more or less rapidly to increase. (See "Etiology of Tumors.")

SECONDARY CHANGES.—The lymphomata do not undergo marked retrograde changes. There is no fatty degeneration, caseation, or softening, such as occurs in scrofulous glands.

PHYSICAL CHARACTERS, ETC.—The physical characters of the lymphomata vary according to the rapidity of their growth. The rapidly-growing forms, in which the cellular elements are so numerous, are of a grayish-white color and soft brain-like consistence, much resembling encephaloid cancer. These often attain an enormous size, and infiltrate the neighboring structures. They have been called by Virchow *lympho-sarcoma*. Those which are more slowly developed, and in which the reticulum constitutes the greater portion of the growth, are much harder in consistence, sometimes being almost cartilaginous. These harder growths rarely attain a large size.

CLINICAL CHARACTERS.—Clinically, the lymphomata are, for the most part, perfectly innocent tumors. They originate most frequently in the lymphatic glands, the gland undergoing a continuous increase in size. Sometimes, as already stated, the enlargement of the glands appears in the first place to be of an inflammatory nature and to result from some irritation, but upon this being removed the glands,

instead of subsiding, continue to increase. In most cases, however, no such source of irritation is discoverable. The glands which are especially prone to this disease, are the cervical, the submaxillary, the axillary, the inguinal, the bronchial and mediastinal, and the abdominal glands. Usually only a single gland, or a single group of glands, is affected; sometimes, however, the growth is more general. As the glands enlarge, they gradually unite, so that ultimately they may form very large lobulated tumors. When occurring in the mediastinum they may invade one or both lungs, and they constitute here the most common form of mediastinal tumor (so-called "Thoracic Cancer"). The lymphatic structures in the intestine may in the same way become enlarged, and project, so as to form polypi.

The lymphomata occasionally, however, exhibit malignant properties. This is especially the case in those richly cellular, soft, rapidly-growing forms which are sometimes met with. Such growths may rapidly infiltrate the surrounding structures, involve the neighboring lymphatic glands, and even infect distant parts. To these malignant forms the term *lymphadenoma* is sometimes applied. They correspond with Virchow's lympho-sarcoma.

In the condition known as "Hodgkin's Disease," and in Leukæmia, lymphomatous growths are met with in various parts of the body.

Hodgkin's Disease.

This disease is characterized by the enlargement of the lymphatic glands in various parts of the body, together with the development of lymphatic growths in internal organs, especially in the spleen; by a diminution in the number of red corpuscles in the blood; and by progressive anæmia. The new growths are precisely similar, histologically, to lymphoma. The disease was formerly described by Hodgkin, Bright, Wilks, and Trousseau, and is called, after the first-named of these observers, "Hodgkin's Disease." Trousseau designated it "Adénie." It is also known as "Anæmia Lymphatica." It is allied to leukæmia, but differs essentially from it in this respect, that the new formation of lymphatic tissue is not associated with any notable increase in the number of the white corpuscles in the blood. (See "Leukæmia.")

The lymphatic glands are usually the earliest seats of the new growth. At first only a single group of glands may be enlarged; subsequently, however, the process becomes more general, and the

glands throughout the whole body may be more or less involved. The groups of glands most frequently affected, in the order of their frequency, are the cervical, the axillary, the inguinal, the retro-peritoneal, the bronchial, the mediastinal, and the mesenteric. The new growth, which in the earlier stages is limited to the glands, gradually breaks through the capsules, so that the enlarged glands become confluent, and form large lobulated masses. The growth may also extend still further beyond the confines of the gland and invade and infiltrate the adjacent structures.

This new growth of lymphatic tissue, which commences in and often extends beyond the confines of the lymphatic glands, is ultimately followed by the formation of lymphatic growths in various internal organs, but more especially in the spleen. The spleen is affected in a large proportion of cases. Here the new growth originates in the Malpighian bodies, and so gives rise to disseminated nodules. These vary in size from minute points to masses as large as a hazel-nut or walnut. They are usually more or less irregular in shape, of a grayish or yellowish-white color, firmer in consistence than the splenic tissue, and not encapsuled. In addition to these, wedge-shaped infarctions surrounded by a zone of hyperæmia are sometimes met with, similar to those which are often seen in leukæmia. The spleen itself is increased in size, although rarely very considerably so; and its capsule is usually thickened, and often adherent to adjacent organs. In quite exceptional cases the spleen is not the seat of these disseminated growths, but is simply uniformly enlarged, like the leukæmic spleen.

The liver, kidneys, alimentary canal, medulla of bone, lungs, and subcutaneous tissue may all become involved, the new growths occurring either as nodules of various sizes scattered through the organs, or in a more infiltrated form, like many of those met with in leukæmia.

Histologically, the new growths are precisely similar to the lymphomata, and like these present differences in the relative proportions of cells and stroma, the richly cellular forms being soft and pulpy, whilst those in which the stroma is more abundant are firmer and more fibrous in consistence. Retrogressive changes rarely occur.

With regard to the pathology of the disease, it is undoubtedly obscure. The development of the new growths cannot in most cases be regarded as the result of infection from a primary centre, as the process is, for the most part, confined to the lymphatic structures, and many and widely distant groups are often simultaneously involved. The dis-

ease thus appears to occupy a different pathological position to that of the malignant tumors. It is probable that there is some special weakness of the lymphatic structures generally which renders them prone to undergo these active developmental changes, the process being determined by some constitutional state or by some local injury of the glands. The progressive anæmia which accompanies, but does not precede, the gland affection, is due to the progressive implication of the lymphatic structures and to the consequent interference with the formation of the blood-corpuscles.

Leukæmia.

In leukæmia, as in Hodgkin's disease, there is usually a development of lymphomatous tissue in various organs. The disease, however, is characterized by the large increase in the number of white corpuscles in the blood, and in the majority of cases by enlargement of the spleen. It is this alteration in the blood which gives leukæmia its distinctive characters—hence its name. The disease will be considered subsequently, when treating of “Diseases of the Blood.”

CHAPTER XIX.

THE MYOMATA, NEUROMATA, AND ANGIOMATA.

The Myomata.

THE Myomata are tumors consisting of muscular tissue. A new formation of muscle has been already described as being frequently associated with the ordinary process of hypertrophy, both of striated and of non-striated muscle—a simple hyperplasia of the elements of the muscle accompanying the increase in their size. (See “Hypertrophy.”)

STRUCTURE.—The myomata consist either of striated or of non-striated muscle. The former are exceedingly rare, only two or three examples having been recorded, and these were congenital.

The myomata of *non-striated* muscle consist, like the physiological tissue, of elongated spindle-cells with rod-shaped nuclei, more or less

isolated or grouped into fasciculi of various sizes, with a varying quantity of connective tissue. The connective tissue is often exceedingly abundant, especially in old tumors, so much so, that these growths in the uterus—where they most frequently occur—have commonly been known as “*fibroid*” tumors. The muscular elements either present a more or less regular arrangement, or pass in all directions through the tumor. The bloodvessels, which are usually not numerous, are distributed in the connective tissue.

DEVELOPMENT.—Striated myoma appears to originate in the urino-genital organs, and to be usually congenital. The much more common non-striated growths probably always originate from muscle. These may form distinctly circumscribed tumors surrounded by a fibrous capsule, or constitute ill-defined irregular masses in the midst of the muscular tissue in which they grow. They not infrequently become pedunculated and form polypi, especially in the uterus.

SECONDARY CHANGES.—Of these, the most frequent is calcification. Hemorrhage, mucoid softening, and the formation of cysts, are also occasionally met with.

Non-striated myomata are most frequently met with in the uterus. They may also occur in the prostate, in the cesophagus, and in the stomach and intestines.

Myoma of Uterus.—The uterus is by far the most frequent seat of myomata, and here they constitute the so-called “uterine fibroid.” In most of these muscular tumors of the uterus there is a large proportion of connective tissue—hence the term “fibroid.” This is especially the case in older growths. Those newly developed, however, consist almost entirely of true muscular tissue. They either form firm hard masses, imbedded in the uterine walls, or project into the uterine or abdominal cavities. When projecting into the uterus they constitute a common form of uterine polypus. These tumors are often multiple. Their growth is slow. The older ones are liable to become calcified. They also sometimes undergo mucoid softening, which gives rise to the formation of cysts in the tumor.

CLINICAL CHARACTERS.—Clinically, the myomata are perfectly innocent.

The Neuromata.

The neuromata are tumors consisting almost entirely of nerve-tissue. The term “neuroma” has been applied to many growths found

in connection with nerves: fibrous, myxomatous, and gummy tumors growing within the nerve-sheath have been included under this head. True neuroma, however, is rarely met with, and is amongst the least frequent of all the new formations.

STRUCTURE.—The neuromata most commonly consist of ordinary medullated nerve-fibres; they therefore resemble in structure the cerebro-spinal nerves, from which they most frequently grow. The nerve-fibres are associated with more or less connective tissue. Virchow has also described as exceedingly rare formations, tumors composed of non-medullated fibres, and of ganglionic nerve-tissue.

DEVELOPMENT.—The neuromata always originate from pre-existing nerve-tissue,—either from the cranial or from the spinal nerves. Their growth is slow, they rarely attain a large size, but usually exist as small single nodules.

The most frequent seat of these growths is the extremities of divided nerves, where they are sometimes found after amputations. They exist, in this situation, as spherical or elongated enlargements of the divided extremity of the nerve; and they are usually intimately connected with the cicatricial tissue of the stump, from which they can only with difficulty be isolated. They may also occur in the course of the nerves in any situation, either as single or multiple nodules.

CLINICAL CHARACTERS.—Clinically, the neuromata are perfectly innocent tumors. They often cause considerable pain.

The Angiomata.

The angiomata, or vascular tumors, are tumors consisting of blood-vessels held together by a small amount of connective tissue. They include the various forms of nævi, the erectile tumors, and aneurism by anastomosis. They may be divided into two classes—the *simple* angiomata, in which the new vessels resemble normal arteries, veins, or capillaries; and the *cavernous* angiomata, in which the blood circulates in a cavernous structure similar to that of the corpus cavernosum penis.

SIMPLE ANGIOMATA.—These include the various forms of nævi, and telangiectasis. They consist of tortuous and dilated blood-vessels, held together by a small quantity of connective and adipose tissue. The vessels are most of them of new formation; some, however, may be the original vessels of the part which have become

considerably enlarged. They most commonly partake of the nature of capillaries, but in other cases the arterial or venous characters predominate. These growths are usually small, superficial, slightly elevated masses; although they sometimes form larger tumors. Their color is red, violet, or purple, according to the character of the blood which they contain. The first-named is much the most frequent.

CAVERNOUS ANGIOMATA.—These include the venous vascular tumors, erectile tumors, and aneurism by anastomosis. They consist of an erectile cavernous tissue, closely resembling that of the corpus cavernosum penis. The growth is made up of irregular fibrous alveoli, which communicate freely with one another, and are lined with an endothelium similar to that of the veins. These spaces are distended with blood, usually venous, which is supplied to them by numerous tortuous vessels, and circulates in them with varying degrees of rapidity. These growths are commonly of a bluish color. They may be diffuse, or form distinctly circumscribed tumors. They often exhibit distinct pulsation. Their favorite seat is the skin and subcutaneous tissue. They may also occur in the orbit, in muscle, and in the liver, spleen, and kidneys.

CHAPTER XX.

THE PAPILOMATA.

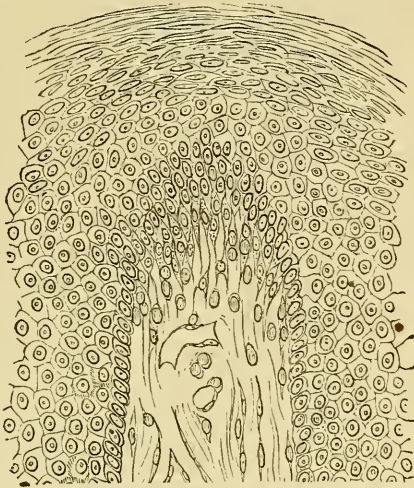
THE Papillomata are new formations resembling in structure ordinary papillæ, and like these they grow from cutaneous, mucous, or serous surfaces.

STRUCTURE.—They consist of a basis of often richly cellular, connective tissue, supporting bloodvessels, which terminate in a capillary network or in a single capillary loop, the whole being enveloped in a covering of epithelium (Fig. 40.) The epithelial covering varies in character in different growths. In those of the skin, it is often very abundant, and the superficial layers are hard and stratified, forming a dense firm covering. In those originating from mucous surfaces, the epithelium forms a thinner investment, and is of a much softer consist-

ence; whilst in those growing from mucous membranes it often constitutes only a single layer.

The growth may be simple—consisting merely of enlarged papillæ, as in a common wart; or it may be complex, the papillæ being very

FIG. 40.



Papilloma.—Showing a single enlarged papilla. (Rindfleisch.)

numerous, and giving off secondary and tertiary offsets. If the investing epithelium be very abundant, it may so inclose the whole mass as to give to it a more or less regular outline. More commonly, however, this is not the case, and the epithelium not being sufficient to fill up the spaces between the papillæ, the growth presents a branched, villous or cauliflower appearance. The bloodvessels are often very numerous, and are sometimes dilated and tortuous.

DEVELOPMENT.—The papillomata always originate from the skin, from mucous, or from serous membranes; and, as already stated, they usually owe their origin to some irritation, and must be regarded as occupying an intermediate position between inflammatory growths and tumors. They most frequently grow from pre-existing papillæ; sometimes, however, they occur where no papillæ exist, springing directly from the sub-epithelial connective tissue:—this is the case in the stomach and larynx. Their growth is usually slow. The individual tumors rarely attain a very large size, the larger forms being for the most part constituted of several smaller growths.

SECONDARY CHANGES.—Of these, ulceration and hemorrhage are the most frequent. They occur especially in those growths which originate from mucous surfaces. The hemorrhage is often very abundant, and may even endanger life. This is not unfrequently the case in the papillary growths of the bladder and intestine.

VARIETIES.—The varieties of papillary tumors depend principally upon their seat. Those growing from the skin include *warts* and *horny growths*. Warts are firm, have a dense epithelial covering, and are less prone to ulceration and hemorrhage than those growing upon other parts. Horny growths appear usually to originate in the sebaceous follicles, by a continuous proliferation of their epithelium. The epithelium, together with the sebaceous secretion, forms a projecting horn, which increases by growth at its base. Such formations hardly come within the definition of papilloma. Larger and more vascular papillary tumors may, however, occur on cutaneous surfaces—such are the *condylomata* and *venereal warts* met with around the anus and upon the external male and female genital organs as the result of irritating secretions.

The papillomata of mucous membranes are softer and more vascular than the preceding; they have a less dense epithelial covering, and are more prone to ulceration and hemorrhage. Many of them come within the category of mucous polypi. They are met with on the tongue, in the larynx and nose, on the gastro-intestinal mucous membrane, on the cervix uteri, and in the bladder. In the bladder and intestine they are often exceedingly vascular, and give rise to profuse hemorrhage. Here they are not unfrequently confounded with villous epithelioma.

Papillomata of serous membranes never form distinct tumors. They are met with most frequently as small outgrowths from the synovial membrane in chronic diseases of joints.

CLINICAL CHARACTERS.—Clinically, the papillomata are innocent growths. They may, however, prove fatal from continuous ulceration and hemorrhage: this is especially the case, as already mentioned, in papillomata of the bladder and intestine. In these situations they are easily mistaken for epithelioma; the symptoms of both are very similar, and it is often only after death that they can be distinguished. In the papillomata the epithelium is *homologous*, being situated only upon the surface of the papillæ, and in no case growing within their connective tissue basis. In the epitheliomata, on the other hand, it

is *heterologous*, and it is met with at the base of the tumor in the subjacent connective tissue. (See Fig. 61.) It is important to remember that a growth which is primarily a simple papilloma may subsequently become an epithelioma. (See "Epithelioma.")

CHAPTER XXI.

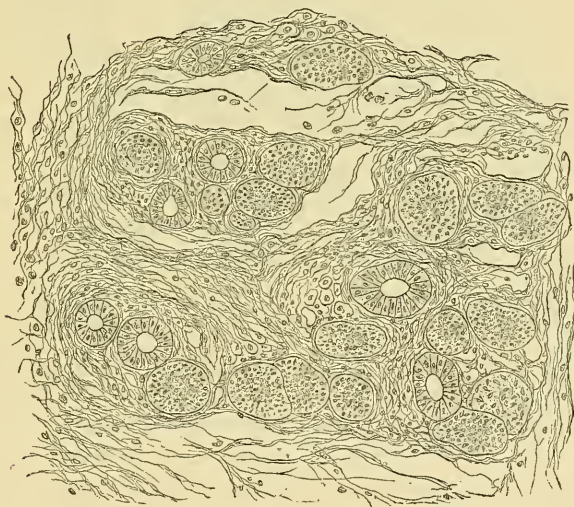
THE ADENOMATA.

THE Adenomata—or, as they are more commonly called, *glandular tumors*—are new formations of gland-tissue.

STRUCTURE.—In structure the adenomata resemble the racemose or tubular glands.

The racemose adenomata consist of numerous small saccules or acini, lined with small epithelial cells, which are often two or three

FIG. 41.



Adenoma of Mamma. $\times 200$, reduced $\frac{1}{2}$.

layers deep. The acini communicate with each other, and are grouped together, being merely separated by connective tissue, in

which are contained the bloodvessels. The connective tissue varies in amount. It may resemble the normal tissue, or if growing rapidly it will be much more richly cellular. It sometimes contains spindle elements. The structure of these tumors is well shown in the accompanying drawing, made from a specimen kindly lent to me by Mr. Cantlie. (Fig. 41.)

Many new growths, however, contain a large amount of this gland-tissue which are not strictly adenomata. All growths originating in glandular organs may be associated with more or less glandular structure. In the mamma, for example, sarcoma, myxoma, and other forms of tumor, are often so intermingled with the gland-tissue of the organ that it becomes difficult to say which is the predominant structure. In many cases it is evident that the development of such tumors is accompanied by an increase of the gland-tissue amongst which they grow. Thus are produced mixed forms—*adeno-fibroma*, *adeno-sarcoma*, *adeno-myxoma*, etc.

The tubular adenomata grow from mucous membranes, and consist of groups of tubules lined with epithelium. They will be again alluded to hereafter.

DEVELOPMENT.—The adenomata always originate from pre-existing gland-structures, of which they are simply local hyperplasias. Their growth, which is usually slow, takes place by the development of diverticula from the saccules or tubules of the gland, and by a proliferation of the inclosed epithelium. The new growth may remain in intimate relation with the adjacent gland, or it may ultimately become separated from it by a fibrous capsule.

SECONDARY CHANGES.—The most frequent of these is fatty degeneration of the epithelium, which may give rise to the formation of small caseous masses in the growth. Dilatation of the saccules and tubules so as to form cysts, and mucoid softening, are also common.

VARIETIES.—*Adenoma of Mamma*.—The mamma is much the most common seat of adenoma. Here two varieties must be distinguished—one, in which there is a general hyperplasia of the whole gland; the other, in which the process is limited to smaller or larger groups of lobules. The former constitutes hypertrophy of the mamma, the latter is the *chronic mammary* or *adenoid* tumor. Pure adenoma of the mamma, however, is not common. (See Fig. 41.) Many tumors in this situation described as adenomata are fibrous, sarcomatous, or myxomatous growths in which is contained a varying amount of gland-tissue. The distinction between such growths and pure adenoma is

often difficult. The adenomata are either superficially or deeply seated in the gland, from which they are usually separated by a loose fibrous capsule. They are commonly round or oval in shape, lobular, and of a hard elastic consistence. On section they often present a lobulated appearance, their racemose structure being sometimes visible to the naked eye.

Adeno-Fibroma and Adeno-Sarcoma of Mamma.—These are more common than pure adenoma. In them the connective tissue between the acini of the gland undergoes active changes, and forms a fibro-cellular, spindle-celled, or round-celled structure, amongst which the acini are embedded. (Fig. 42.) In many cases it is difficult to

FIG. 42.



Adeno-Fibroma of Mamma.—Showing new growth of gland structure and of connective tissue.
 $\times 100$, reduced $\frac{1}{2}$.

determine whether the glandular structure is really increased in amount, whilst in others it is so abundant that such is evidently the case. These tumors form lobulated masses of a firm consistence. They grow slowly, and rarely ulcerate. In most cases they contain cysts. Many of these are lined with cylindrical epithelium and are formed by the dilatation of the ducts of the gland; others appear to originate from localized softenings of the tissue. These cysts are usually very numerous, and they often attain a large size. They are

frequently seen much flattened, so as to present the appearance of fissures running amongst the growth. In other cases they are more or less completely filled by masses of the tumor which have grown into their interior. This formation of cysts in these tumors has given rise to the terms *cystic-sarcoma*, *cystic-adenoma*, etc.

Adenoma of Mucous Membranes.—The glandular structures of mucous membranes are also common seats of adenoid growths, and here they are usually of the tubular variety. In the nose, the pharynx, the stomach, the intestines, the vagina and uterus, these growths are sometimes met with. In course of time they usually gradually project above the surface of the membrane so as to form a polypus, and thus constitute one of the forms of *mucous polypi*. In consistence they are soft and somewhat gelatinous, and often present a semi-translucent appearance. Their surface resembles in color the surrounding mucous membrane. The formation in them of cysts, by the dilatation of their tubules, is exceedingly frequent: the cysts usually contain a soft mucoid substance. Adenoma of mucous membranes often becomes cancerous (see “Cylindrical Epithelioma,” or “Adenoid Cancer”).

CLINICAL CHARACTERS.—Clinically, the adenomata are perfectly innocent; they are, however, very liable to be confounded with growths possessing malignant properties. A tumor, also, which is primarily a simple adenoma, may subsequently become cancerous. The anatomical distinction between carcinoma of a gland in its earlier stages and a simple glandular tumor is often exceedingly difficult, especially in the mamma and mucous membranes. In cancer the growth appears to commence by a proliferation of the epithelium within the ducts of the gland, and as the epithelium only subsequently becomes heteroplastic, the determination of the nature of the tumor in this stage is necessarily attended with considerable difficulty. This will be again alluded to when speaking of cancer. (See “Structure of Carcinoma.”) In sarcomatous tumors, again, originating in the connective tissue of a gland, the ducts of the gland, filled with epithelium, are often seen embedded in the new growth, and thus the appearance of adenoma may be closely simulated.

CHAPTER XXII.

THE SARCOMATA.

THE Sarcomata are tumors consisting of embryonic connective tissue. Of these there are several varieties, depending upon the size and configuration of the cells, and the nature of the intercellular substance. They include what have generally been known in this country as *fibro-plastic*, *fibro-nucleated*, *recurrent-fibroid*, and *myeloid* tumors. Many growths formerly described as "cancers" also belong to this class of new formations.

Connective tissue in its embryonic condition is an immature tissue in a state of rapid development. In its most immature state it differs from the fully developed tissue in consisting almost entirely of small round cells, whilst its intercellular substance, instead of being fibrous, is soft and amorphous. This is the common condition of connective tissue in the primary stages of all rapid formative processes, as already described when speaking of it as the tissue from which many tumors of the connective-tissue class originate. (See "Development of Tumors.")

In the process of development of this embryonic into mature connective tissue, the cells diminish in number, many of them assume a spindle shape, and the intercellular substance fibrillates. Similar changes are seen in inflammatory conditions of connective tissue. Here also many of the small round cells which constitute the "granulation tissue" become spindle cells, and the granulation tissue ultimately develops into the fibrous tissue of the cicatrix. In the sarcomata, however, the connective tissue retains the embryonic state throughout its growth, there is a progressive formation of embryonic tissue; and although the process of development may occasionally proceed in certain parts of the tumor to the formation of a more highly developed structure, as fibrous tissue, cartilage, or bone, so that a mixed form of tumor is produced, it usually ceases at the embryonic stage.

STRUCTURE.—The sarcomata may thus be defined as tumors consisting of connective tissue which throughout its growth retains the embryonic type. The *cells*, which constitute nearly the whole of the

growth, consist for the most part of masses of nucleated protoplasm, and rarely possess a limiting membrane. They present many variations in size and form; as a rule, however, they preserve the same general characters in the same tumor. There are three principal varieties—the *round*, the *fusiform*, and the *myeloid* cells.



Cells from a Spindle-celled Sarcoma. $\times 350$.

The *round* cells are many of them indistinguishable from lymph-cells or white blood-corpuscles. Others are somewhat larger and contain an indistinct nucleus with one or more bright nucleoli: these more closely resemble the cells of a granulation.

The *fusiform*, or *spindle-shaped* cells are the so-called “fibro-plastic cells.” (Fig. 43.) They are long narrow cells, terminating at each end in a fine prolongation. Some of them may be broader, approaching the epithelial type; others more or less stellate. They are sometimes slightly granular, and they inclose a long oval nucleus, with or without nucleoli. In size they vary considerably. These cells represent a higher state of development than the round cells, resembling those met with in embryonic tissue which is in the process of forming mature connective tissue. (See Fig. 97, B.)

The *myeloid*, or mother cells, are much larger than either of the preceding, and are analogous to the cells met with in the medulla of the foetal bone. (See Fig. 51.) They are large irregular-shaped masses of nucleated protoplasm, for the most part more or less spherical, and often possessing numerous offshoots. They are finely granular, and contain several round or roundly-oval nuclei, each with one or more bright nucleoli. The nuclei may be exceedingly numerous, one cell containing as many as thirty. Both the cells and nuclei vary considerably in size.

An *intercellular substance* exists in all the sarcomata, although it is usually small in quantity, the cells lying in nearly close apposition. It may be perfectly fluid and homogeneous, or firmer and granular, or more or less fibrillated. Chemically it yields albumen, gelatine, or mucin.

The *bloodvessels* are usually very numerous, and are either in direct contact with the cells, or separated from them by a little fibrillated tissue. Their distribution is very irregular, and their walls often consist of embryonic tissue similar to that of the growth which they

supply; hence the frequency with which rupture and extravasation of blood take place.

DEVELOPMENT.—The sarcomata always originate from connective tissue—either from the subcutaneous, the submucous, or the subserous tissues, the fasciæ, the connective tissue of organs, the periosteum, or the medullary tissue of bones. Their growth is usually diffuse: they increase by the continuous invasion of their connective-tissue matrix, so that no line of demarcation exists between the two. They frequently also invade other tissues, the elements of the growth extending for some distance into the surrounding structure. This infiltrating tendency of the sarcomata varies considerably in the different varieties, being much more marked in the round-celled than in the spindle-celled myeloid growths. A circumscribed growth is less common. A sarcomatous tumor, however, often becomes encapsuled, and growth takes place within the capsule; but even in this case the capsule is sometimes merely that of the part within which the growth originates, as the periosteum, or the capsule of a lymphatic gland.

SECONDARY CHANGES.—The most important of these is fatty degeneration. This always occurs to a greater or less extent in the older portions of the growth, causing softening, or the production of cyst-like cavities. It is frequently associated with destruction of the bloodvessels and hemorrhage: the latter may give rise to the formation of sanguineous cysts. (See “Blood-Cysts.”) Calcification, ossification, and mucoid degeneration are less common. The occurrence of calcification, ossification, and pigmentation is influenced by the predisposition of the matrix from which the growth is produced:—thus, calcification and ossification are more prone to occur in tumors originating in connection with bone, pigmentation in those originating from the cutis or eyeball.

VARIETIES.—Although all the sarcomata possess the same general characters, they present many histological and clinical differences which may serve as bases for their classification. The occurrence of various secondary changes—pigmentation, mucoid degeneration, and the formation of cysts, impart their respective characters to the growth: hence *melanotic-sarcoma* and *cystic-sarcoma* have been described as distinct varieties. This is to a certain extent justifiable, inasmuch as sarcomata which have undergone these transformations, in many cases possess the property of reproducing the same characters, when they occur secondarily in other parts. Then, again, as already stated, sarcomatous tumors are sometimes complex in their structure, and

are associated with other tissues belonging to the connective-tissue group. A combination of sarcoma with fatty, cartilaginous, osseous, and mucous tissue, is thus not uncommonly met with. This is owing to the embryonic tissue exhibiting a tendency to develop into the different varieties of connective-tissue. (See "The Tumors.") The mixed forms—*chondro-sarcoma*, *osteo-sarcoma*, *myxo-sarcoma*, etc., are thus produced. The following histological classification, based upon the three different forms of cells already described, is the one generally adopted. It must, however, be borne in mind, that all the varieties of cells may be found in the same tumor, although the majority are usually of the same type; hence, the *majority* will determine the class to which the growth belongs.

Spindle-celled Sarcoma.

These tumors, which include the growths described by Paget in this country as "fibro-plastic," and "recurrent fibroid," are the most common of all the sarcomata. They consist mainly of spindle-shaped and fusiform cells lying nearly in close contact, with a little homogeneous or slightly fibrillated intercellular substance. The cells, which contain well-marked oval nuclei, with one or more nucleoli, are parallel to one another, and are arranged in bundles which pass in all directions through the growth, often giving to it a somewhat fibrous appearance. In those portions of the section in which the bundles of spindle-elements have been cut transversely, they present the appearance of round cells. The cells vary considerably in size in different tumors, hence the division into *small* and *large* spindle-celled growths.

FIG. 44.



Small Spindle-celled Sarcoma.—From a tumor of the leg. $\times 200$.

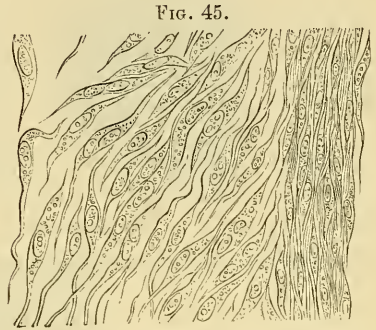
Small Spindle-celled Sarcoma.—In these the cellular elements are small, often not more than $\frac{1}{1500}$ th inch in length, and the intercellular substance is occasionally imperfectly fibrillated.

(Fig. 44.) These growths approach therefore

the confines of the fibromata, and histologically they must be regarded as occupying an intermediate place between embryonic and fully-developed connective tissue. They grow from the periosteum, the fasciæ, and from connective tissue in other parts. They are usually tolerably firm in consistence, of a whitish or pinkish-white color, and for the most part present, on section, a translucent somewhat fibrillated ap-

pearance. They are often encapsuled, much more frequently so than the varieties of sarcoma, but they are very liable to infiltrate the surrounding structures, and to recur locally after removal.

Large Spindle-celled Sarcoma.—The cellular elements in these tumors are much larger than in the preceding. The cells are plumper, and the nuclei and nucleoli are especially prominent, and frequently multiple. (Fig. 45.) The intercellular substance is more scanty, and there is a complete absence of any fibrillation. These growths are much softer in consistence than the small-celled variety. They are of a pinkish-white color, and are often stained by extravasations of blood, and sometimes in parts are almost diffuent from extensive fatty degeneration. They grow rapidly, and are usually exceedingly malignant.



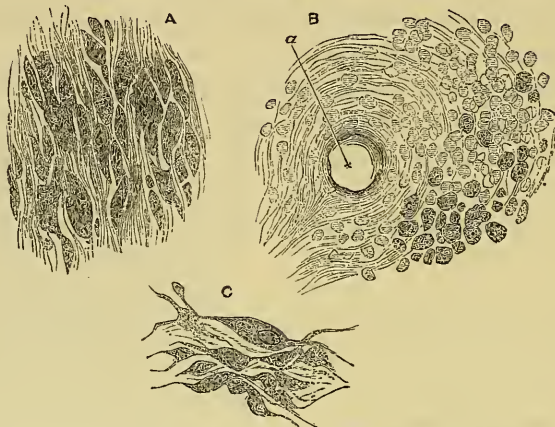
Large Spindle-celled Sarcoma.—To the left—the cells have been separated by teasing, so that their individual forms are apparent; to the right—they are in their natural state of apposition, such as would be seen in a thin section of the tumor. (Virchow.)

MELANOTIC SARCOMA.—This is a variety of sarcoma in which many of the cells contain granules of dark-colored pigment. By far the greater number of melanotic tumors are sarcomata, and most of the growths which were formerly described as “melanotic cancers,” belong in reality to this class of new formations. Not only are these melanotic tumors most frequently sarcomata, but the majority of them consist mainly of spindle-shaped cells—hence they are described in the present section.

The melanotic sarcomata originate principally in two situations—in the choroid coat of the eye, and in the superficial integuments. In both of these situations pigment is a normal constituent of the tissues, and this tendency of structures normally containing pigment to originate melanotic growths, is exceedingly characteristic. (See “Pigmentary Degeneration.”) These tumors usually consist of spindle-shaped cells, although in some cases the prevailing type of their elements is round or oval. (Fig. 46.) The pigment, which gives to them their distinctive characters, consists of granules of a brownish or dark sepia color, which are distributed within the cells. (Fig. 46, c.) Frequently only, a very small proportion of the cells are pigmented, whilst in other tumors the pigmentation is much more universal; in

all cases, however, a large number of the elements will be found to be quite free from pigment.

FIG. 46.



A Melanotic Sarcoma of the Penis.—A. A thin section, showing the general arrangement of the elements. $\times 200$. B. A section from the peripheral part of the growth, showing the “indifferent cells,” amongst which are small isolated pigmented elements. At *a*, a bloodvessel is seen. $\times 200$. C. Some of the elements separated by teasing. In these the pigment granules are well seen. $\times 400$.

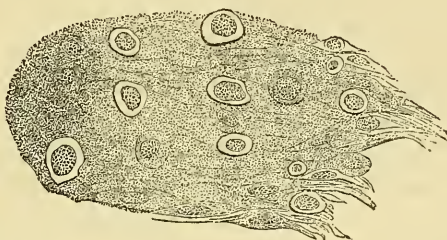
These melanotic tumors are amongst the most malignant of the sarcomatous growths. Although they have comparatively but little tendency to extend locally, they are disseminated by means of the bloodvessels, and occasionally also by the lymphatics, and thus reproduce themselves often very rapidly in distant tissues. In doing so, although they almost invariably maintain their melanotic characters, the degree of the pigmentation of the secondary tumors varies considerably. Whilst many of them may be perfectly black in color, others may be much paler, and perhaps only partially streaked with pigment. The secondary growths are soft, usually distinctly circumscribed, and often encapsuled. They may occur in almost every organ of the body—the liver, the spleen, the kidneys, the lungs, the heart, the brain, and spinal cord, and also the lymphatic glands and subcutaneous tissue, may all be simultaneously involved. I have observed, that when occurring in internal organs, the pigmentation is not always limited to the secondary nodules, but that many of the cells proper to the organ itself are filled with granules of similar pigment, which is most abundant in those cells which are immediately adjacent to the new growth. This pigmentation of the cells of the

organ often extends for some distance beyond the confines of the tumor.

OSTEOID SARCOMA.—This, which is often known as “osteoid cancer,” is a variety of sarcoma (usually of spindle-celled sarcoma) in which the growth is either more or less calcified, or has partially become converted into true bone. As a primary growth it is met with almost exclusively in connection with bone, growing either from the periosteum or the medulla. The osteoid characters are usually reproduced in the secondary tumors occurring in the lungs and in other parts.

Simple calcification is much more common than true ossification. Here the growth merely becomes infiltrated with calcareous salts, which may be dissolved out with a little dilute hydrochloric acid, when the characteristic sarcomatous structure becomes revealed. In

FIG. 47.



Osteoid Sarcoma.—From a secondary tumor of the lung. Showing the calcification of a spindle-celled growth, and the formation of broad bands of calcified intercellular material inclosing spaces which contain round and oval cells. $\times 200$.

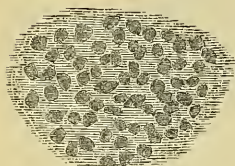
other cases this calcification is associated with the conversion of portions of the tumor into true, although usually imperfect, bone. When this has occurred, there will be seen amongst the spindle-shaped, round, or myeloid elements, tracts of tissue consisting of broad bands of granular intercellular material, infiltrated with calcareous salts, inclosing spaces which contain spindle, oval, or round cells. (Fig. 47.) This structure often much resembles cartilage. In other parts of the growth, where the change is more advanced, may be seen lacunæ and even canaliculi such as are found in true bone.

In these osteoid growths it is most important to recognize the existence of the sarcomatous element, inasmuch as it is the presence or absence of this which determines the innocent or malignant nature of the growth. Osteoid sarcoma must be carefully distinguished from the simple osseous tumor.

Round-celled Sarcoma.

This is of softer consistence than the spindle-celled growths, and from its frequent resemblance in physical characters to encephaloid,

FIG. 48.



Round-celled Sarcoma.—
A thin section of a small
round-celled sarcoma of the
liver. $\times 200$.

it is sometimes known as “medullary,” “encephaloid,” or “soft” sarcoma. Histologically, it is elementary embryonic tissue, consisting mainly of the round cells already described, embedded in a scanty and usually soft, homogeneous, or finely granular intercellular substance. (Fig. 48.) The cells usually resemble those met with in the most elementary embryonic tissue; less frequently, they are larger, and contain large round or oval nuclei, with bright nucleoli. There is an almost complete

absence of fusiform cells, and of the partial fibrillation which is so frequent in the more highly developed spindle-celled variety.

The round-celled sarcomata are of a uniform, soft, brain-like consistence, somewhat translucent or opaque, and of a grayish or reddish-white color. On scraping the cut surface, they yield a juice which is rich in cells. They are exceedingly vascular, the vessels often being dilated and varicose, and from their liability to rupture, they frequently give rise to ecchymoses and to the formation of sanguineous cysts. (See “Blood Cysts.”) They grow from the cutis, the subcutaneous cellular tissue, the periosteum, the fasciæ, and from the connective tissue of organs. They extend rapidly by peripheral growth, infiltrate the surrounding structures, reproduce themselves in internal organs, and often involve the lymphatic glands. From their clinical and physical characters, these tumors are very liable to be confounded with encephaloid cancer:—they are distinguished by the absence of an alveolar stroma, and by the uniformity in the character of their cells.

GLIOMA.—This is a variety of round-celled sarcoma growing from the neuroglia or connective tissue of nerve. It consists of very small round cells, embedded in an exceedingly scanty, homogeneous, granular, or slightly fibrillated intercellular substance. (Fig 49, *a*.) Some of the cells may possess fine prolongations which, by communicating with one another, form a somewhat reticulated structure. These tumors occur in the gray and white substance of the brain, in the cranial nerves, and in the retina. In the retina they usually com-

mence as a minute nodule, which may gradually increase until it projects as a large fungating tumor from the orbit. They are not encapsuled, and although they may occasionally infiltrate the tissues in which they lie and cause secondary growths in their immediate

FIG. 49.

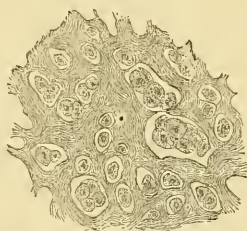


Sarcomatous Tumors from the Brain—*a*. A glioma of cerebellum. This represents the appearance ordinarily presented by these growths. *b*. A comparatively rare form of sarcoma, which consists of large nucleated cells inclosed within the meshes of a vascular network. The development of this tumor took place in the brain subsequently to that of spindle-celled growths—primarily in the thigh, and secondarily in the lung. $\times 200$.

vicinity, they very rarely reproduce themselves in the lymphatic glands or in internal organs. They are liable to small hemorrhages into their structure, and sometimes become more or less caseous.

ALVEOLAR SARCOMA.—This is a rare form of round-celled sarcoma, which was first described by Billroth. The cells, which are large, sharply defined, round or oval in shape, and inclose prominent round nuclei, are separated from each other by a more or less marked fibrous stroma. In some parts this stroma forms small alveoli within which the cells are grouped; but careful examination will always show that in most parts of the section the stroma really penetrates between each individual cell. It is this last-named character which serves to distinguish these tumors from the cancers, with which, in many cases, they may easily be confounded. The accompanying drawing, made from a preparation kindly lent to me by Mr. R. J. Godlee, shows well their microscopical characters. (Fig. 50.)

FIG. 50.



Alveolar Sarcoma.—From a tumor of the skin. $\times 200$.

Alveolar sarcomata are met with principally in the skin, bones, and muscles. In the skin, where they are often multiple, they lead to ulceration. They tend to recur locally, and also to reproduce themselves in internal organs.

Myeloid Sarcoma.

This, which is the well-known *myeloid* tumor, is somewhat allied to the spindle-celled growths. It possesses, however, certain histological peculiarities which probably depend upon the characters of the

FIG. 51.



Myeloid Sarcoma. (Virchow.)

tissue from which it grows. Myeloid tumors nearly always occur in connection with bone, and most frequently originate in the medullary cavity. They consist of the large, many nucleated cells already described as “myeloid cells,”—which resemble the cells of the medulla in a state of excessive nutritive activity—together with numerous fusiform cells like those met with in the spindle-celled varieties. There are also some smaller round and oval elements. The large myeloid cells which give to these tumors their distinctive characters, are usually much more numerous in those growths which originate in the medullary cavity than in those which spring from the periosteum. These various forms of cells are nearly in close contact, there being very little intercellular substance. (Fig. 51.) The growths are

sometimes very vascular, so much as to give rise to distinct pulsation. They often contain cysts.

Myeloid tumors almost always grow in connection with bone, the heads of the long bones being their favorite seat. They are also frequently met with springing from the periosteum of the upper and lower jaws, where they constitute one form of *epulis*. When originating within the medullary cavity, the compact tissue of the bone becomes expanded over them, and they thus often communicate on palpation the peculiar sensation known to surgeons as "egg-shell cracking." These tumors are for the most part of firmer consistence than the other varieties of sarcoma; many of them are firm and fleshy, although others are softer, more resembling size-gelatin. They are not pulpy and grumous like the soft sarcomata, neither do they present the fasciculated appearance of the spindle-celled varieties. Their cut surface has a uniform succulent appearance, often mottled with patches of red. They are often encapsuled by the periosteal covering of the bone from which they grow. They are rare after middle life, and are the least malignant of all the sarcomata.

Blood-Cysts.

Tumors are occasionally met with into which so much hemorrhage has taken place as to mask their real nature, and to give to them the appearance of blood-cysts. The nature of these blood-cysts has only recently been understood. They are now known to be in the majority of cases soft, round, or spindle-celled sarcomata. They consist of broken down blood coagula, surrounded by an ill-defined layer of soft sarcoma tissue. The microscope will also usually reveal sarcomatous elements amongst the altered blood. These growths are exceedingly malignant, and hence the recognition of their sarcomatous origin is all important.

Clinical Characters of the Sarcomata.

The sarcomata occur most frequently in early and middle life, and, next to the carcinomata, are the most malignant of the new formations. They are especially characterized by their great tendency to extend locally and to infiltrate the surrounding structures, so that they are exceedingly prone to recur *in loco* after removal. They comparatively rarely infect the lymphatic glands, and in this respect present a marked

contrast to the cancers. They are also very liable to become generally disseminated, although this is not usual in the earlier stages of the disease. The secondary growths occur most frequently in the lungs. The dissemination is effected by means of the blood, and this is owing to the thinness of the walls of their bloodvessels and to the immediate contact of these with the cells of the growth—conditions most favorable to the entrance of the cellular elements into the circulation. The dissemination of the sarcomata is, on this account, sometimes more rapid than that of the carcinomata. In the latter, extension in the early stage takes place principally by the lymphatics, and dissemination by the blood only occurs later in the disease. The secondary sarcomata usually resemble the primary one, but in exceptional cases the several varieties may replace one another.

These malignant properties, as has been seen, are possessed by the different varieties of sarcoma in very different degrees. As a rule, the softer and more vascular the tumor, and the less its tendency to form a fully developed tissue, the greater is its malignancy. The soft, round celled, and large spindle-celled varieties are thus usually much more malignant than the firmer, small spindle-celled growths. Their infiltrating powers are much greater, they sometimes infect the lymphatic glands, and tend to reproduce themselves very rapidly in internal organs. Many of the small spindle-celled tumors, after removal, never recur, whilst others recur locally several times, and ultimately reproduce themselves in distant parts. As a rule, largeness of the spindle elements and the existence in many of them of more than one nucleus; is an evidence of special malignancy. The presence of a capsule limiting the growth must also be taken into account in judging of the degree of its malignancy. It must, however, be borne in mind that in a growth distinctly encapsuled, the sarcomatous elements may invade the adjacent structures. The myeloid growths are the least malignant; they may however also, in exceptional cases, give rise to secondary growths in internal organs.

CHAPTER XXIII.

THE CARCINOMATA.

THE Carcinomata, or Cancers, are new formations consisting of cells of an epithelial type, without any intercellular substance, grouped together irregularly within the alveoli of a more or less dense fibroid stroma.

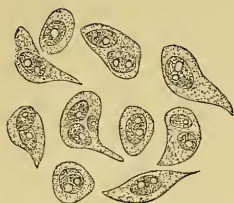
The term "*cancer*" has been so commonly applied indefinitely to any growth possessing malignant properties that "*cancerous*" and "*malignant*" have come to be regarded by many as synonymous terms. It is important however clearly to distinguish between them. A *cancer* is a growth possessing the above-named definite structure; a *malignant* growth, on the other hand, is one which, independently of its structure, tends to reproduce itself in adjacent or distant tissues. (See "Malignancy.") "*Cancerous*" is an *anatomical* term; "*malignant*" is a *clinical* one.

The Carcinomata include the four following varieties: *Scirrhus*, *Encephaloid*, *Colloid*, *Epithelioma*. Of these, the first three possess the same general characters, although they present certain structural and clinical differences which serve to distinguish them. Epithelioma constitutes a more distinct variety. It will be well, in the first place to describe the characters common to the larger and more important group, and then those which are peculiar to its individual members. Epithelioma will be considered subsequently.

STRUCTURE.—In structure scirrhus, encephaloid, and colloid cancer so far resemble one another, that they all consist of cells of an epithelial type, without any intercellular substance, grouped together irregularly within the alveoli of a fibrous stroma. (See Fig. 55.) Although there is no intercellular substance, a certain amount of liquid exists between the cells. It is this liquid which exudes from the freshly-cut surface of the cancer, and the number of cells which it contains give to it a milky appearance.

The *cells* are characterized by their large size, by the diversity of their forms, and by the magnitude and prominence of their nuclei and nucleoli. (Fig. 52.) In size they vary from $\frac{1}{600}$ to $\frac{1}{1500}$ of an inch

FIG. 52.

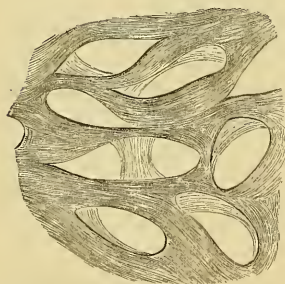


Cells from a *Scirrhus* of
the *Mamma*. $\times 350$.

in diameter; the majority being about five times as large as a red blood-corpuscle. They are round, oval, fusiform, caudate, polygonal—exhibiting, in short, every diversity of outline. These variations in form are principally owing to the mutual pressure to which in their growth they are subjected. The nuclei, which are large and prominent, are round or oval in shape, and contain one or more bright nucleoli. The nuclei are, perhaps, most frequently single; two, however, are frequently met with, and in the softer and more rapidly growing cancers they may be more numerous. The cells rapidly undergo retrogressive changes, hence they usually contain molecular fat. They are many of them exceedingly destructible, so that sometimes more free nuclei than cells are visible. Cells precisely similar to these are met with in other morbid growths, and also in the normal tissues. There is thus no *specific* “cancer-cell.” It is the general character of the cells, together with their mode of distribution in the meshes of a fibroid stroma, that determines the nature of the growth to which they belong. The appearance presented by these cells grouped within the alveoli of the cancer sometimes closely simulates, in the earlier stages of growth, that of simple adenoma. (See Fig. 41.) In adenoma, however, the cells resemble the epithelium of the gland; they are smaller, and less irregular in size and shape, and less closely packed than those of carcinoma. In many cases, indeed, they form merely a single layer lining the walls of the acini.

The *stroma* varies considerably in amount, being much more abundant

FIG. 53.



The *Alveolar Stroma* from a
Scirrhus of the *Mamma*.—The cells
have been removed by pencilling.
 $\times 200$.

in some varieties of cancer than in others. It consists of a more or less distinctly fibrillated tissue arranged so as to form alveoli of various forms and sizes, within which the cells are grouped. (Figs. 53 and 55.) These alveoli communicate with one another, so as to form a continuous cavernous system. The characters of the stroma vary with the rapidity of its growth:—if this is rapid it will contain some round and spindle-shaped cells (see Fig. 57); if, on the other hand, it is slow or has altogether ceased, the tissue will

contain but few cells and will be denser and more fibrous in character. The latter is the condition in which it is most commonly met with.

Within the stroma are contained the *bloodvessels*. These are often very numerous, and form a close network. They are limited to the stroma, and only in very exceptional cases do they encroach upon the alveoli.¹ This distribution of the bloodvessels is important, as distinguishing the carcinomata from the sarcomata. In the latter, the vessels are not supported by a stroma, but ramify amongst the cells of the growth; hence the facility with which these tumors become generally disseminated.

In addition to the bloodvessels, the carcinomata also possess *lymphatics*. These accompany the bloodvessels, and, as has been shown by MM. Cornil and Ranvier, communicate freely with the alveoli. This explains the great tendency of cancer to infect the lymphatic glands.

DEVELOPMENT.—The question of the genesis of carcinoma involves that of the genesis of epithelium generally. It is maintained by many histologists that epithelium can only originate from epithelium, and that the strata of cells set aside in the embryo for the production of the epithelial tissues is the source from which all epithelium is subsequently derived. Others admit that epithelium may also originate from connective tissue. (See "Development of Tumors.") A like difference of opinion exists as to the source of the epithelioid cells of cancer. By many—as Waldeyer, Thiersch, and Billroth—they are regarded as originating only from pre-existing epithelium. Others—amongst whom are Virchow, Lücke, Rindfleisch, and Klebs—maintain that they may also be derived from cells belonging to the connective tissue. It is also believed by some—as Köster—that many cancers originate from the endothelium of the lymphatics.

The difficulty of determining the genesis of carcinoma is partly owing to the fact that it usually originates in structures where epithelium is normally abundant, as in the mamma, skin, and alimentary canal; and that this normal epithelium is always, from the earliest stage of the growth, the seat of active proliferation. In cancer of the mamma, for example, the first change often observable is an accumulation of epithelium within the ducts of the gland, a condition very

¹ In soft rapidly growing cancers the bloodvessels have occasionally been observed to project as tufts into the alveoli. See case reported by Mr. Marcus Beck and Mr. Arnott, Trans. Path. Soc. Lond., 1874, p. 224.

similar to that already described as occurring in the development of an ordinary glandular tumor. (See "Adenoma.") Soon, however, the epithelium alters its characters. The cells become larger and more irregular in shape, and their nuclei are more prominent. The epithelium is then found outside the ducts, amongst the inter- and peri-glandular connective tissue, which is also in a state of active proliferation, and is infiltrated with small round cells. The outline of the ducts ultimately becomes completely annihilated, and the epithelioid cells are seen in alveoli formed of a fibroid tissue. The question arises as to whether the epithelioid cells, which constitute the ultimate cancerous growth, originated from the epithelium normally existing within the ducts of the gland, which in the process of development has extended beyond the ducts in the surrounding tissue; or, whether they originated from the proliferating elements of the connective tissue. Although this question cannot be regarded as finally settled, it is tolerably certain that primarily, at all events, carcinoma in all cases originates from epithelium; and from the investigations of Prof. Maier and Dr. Creighton, already alluded to, it is probable that the epithelial growth having attained a certain degree of development becomes infective, and exercises an influence upon the proliferating cells of the connective tissue (influence of contact), which causes them gradually to assume an epithelial type. The doctrine of the primary epithelial origin of the carcinoma is now steadily gaining ground. The tendency which is exhibited by the cells of cancerous growths to maintain the type of the epithelial structures in the vicinity of which they grow is greatly in favor of it. In cancers situated near the cutaneous surfaces, for example, the cells are usually of the squamous type, whereas in those growing in connection with the glands of mucous membranes, they more commonly resemble the epithelium of the gland. In adopting this doctrine of the origin of carcinoma it is obviously impossible to admit the occurrence of primary growths in situations where no epithelium normally exists—as in bone and muscle; and we now know that tumors in these tissues which were formerly described as cancers, are in reality sarcomata.

The *stroma* of carcinoma is partly the pre-existing connective tissue of the part in which the cancer originates, and partly a new formation. The new growth may probably be regarded as the result of the irritation of the connective tissue by the infiltrating epithelial cells. The alveoli are formed by the linear or more globular grouping of the epithelium amongst the meshes of the stroma.

The carcinomata in their growth never become encapsuled, but gradually infiltrate the surrounding structures. This process of infiltration is very characteristic, and is more marked in cancer than in any of the malignant growths. A zone of small-celled infiltration is seen for some distance around the confines of the tumor, so that there is no line of demarcation between it and the normal structures. (See Fig. 54.)

SECONDARY CHANGES.—The most important of these is fatty degeneration. This always occurs to a greater or less extent in all the varieties of carcinoma. The more rapid the growth, the earlier does this retrogressive change take place, and the greater is its extent; hence it is usually most marked in encephaloid. It produces softening of the growth, which is often reduced to a pulpy cream-like consistence. Pigmentation, mucoid and colloid degeneration may also occur. Calcification is very rarely met with.

VARIETIES.—The term “cancer” was so vaguely applied by the older pathologists—nearly all malignant formations being included under this head—that considerable confusion has resulted in the classification of cancerous growths. Peculiarities in situation, structure, and appearance have given rise to special names, hence the terms—“osteoid,” “chondroid,” “cystic,” “villous,” and “hæmatoid” cancer. A cancer containing large quantities of pigment was described as a distinct variety, under the name of *melanotic* cancer. Melanotic cancer, however, is comparatively rare. The majority of tumors which are thus designated are in reality sarcomata. (See “Melanotic Sarcoma.”)

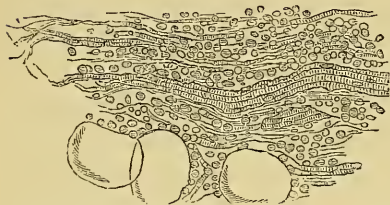
The most convenient classification, and that which is now generally adopted, divides the carcinomata into four groups: *scirrhous*, *fibrous*, or *chronic* cancer; *encephaloid*, *medullary*, or *acute* cancer; *colloid* or *gelatiniform* cancer; and *epithelial* cancer, or *epithelioma*, including *adenoid* cancer. This division is based principally upon the relative proportion of the stroma, and upon the type of the epithelial elements.

Scirrhous Cancer.

Scirrhous, *fibrous*, or *chronic* cancer is characterized by the large amount of its stroma and by the chronicity of its growth. The slowness in the development of scirrhous probably accounts in great measure for the peculiarities in its structure and physical characters.

The epithelial growth, although at first it may be luxuriant, quickly subsides. The elements soon atrophy and undergo retrogressive changes. They are most abundant in the external portions of the tumor, where growth is taking place; in the central portions they may be almost entirely wanting. The accompanying figures (Figs. 54 and 55) show the appearances presented by scirrhus of the mamma in the earlier stages of its development.

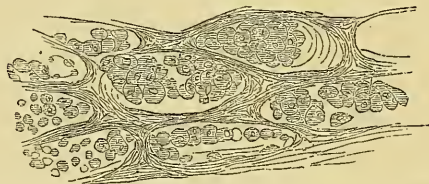
FIG. 54.



Scirrhus of the Mamma.—A thin section from the most external portion of the tumor, showing the small-celled infiltration ("indifferent tissue") of the muscular fibres and adipose tissue in the neighborhood of the gland. $\times 200$.

stroma, and to the subsequent induration and contraction which it undergoes. It quickly assumes the characters of cicatricial tissue, and becomes hard and indurated. This causes obstruction and obliteration of the bloodvessels which it contains, and it is probably to this interference with the vascular supply that the arrest in the development of the cancer is owing. The whole of the central por-

FIG. 55.



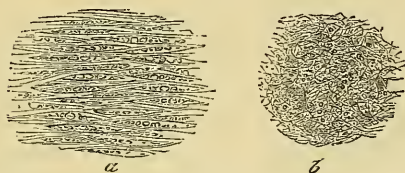
Scirrhus of the Mamma.—A portion of the tumor somewhat internal to that represented in Fig. 54, showing the characteristic alveolar structure of the cancer. $\times 200$.

tions of the growth may thus ultimately consist simply of dense fibroid tissue, amongst which are contained atrophied epithelial cells and fatty debris (Fig. 56), the periphery being the only part where the epithelial structure is visible. The amount of atrophy and contraction varies considerably in different cases.

The physical characters of scirrhus are in the same way due to the abundance of its stroma. The growth is firm and hard, and it is usually depressed in the centre, owing to the contraction of the fibroid tissue; this is very characteristic of scirrhus of the breast,

where it causes puckering of the superjacent structures. On section, the tumor presents a grayish-white glistening surface, sometimes

FIG. 56.



Scirrhus of the Mamma.—A section from the more central portions of the tumor, showing the atrophy of the epithelial cells, the diminution in the size of the alveoli, the fibroid tissue, and the fatty débris. *a*, earlier stage; *b*, more advanced. $\times 200$.

intersected with fibrous bands. The more external are less firm than the central portions of the growth, and yield, on scraping, a juice which is rich in nucleated cells, free nuclei, and granules.

Scirrhus is most commonly met with in the female breast, and in the alimentary canal—especially in the œsophagus, pylorus, and rectum. It also occasionally occurs in the skin. The secondary growths to which it gives rise are often encephaloid.

Encephaloid Cancer.

Encephaloid, *medullary*, or *acute* cancer, is very closely allied to the preceding, from which it differs merely in the greater rapidity of its growth, and the consequent small amount of its stroma, and the softness of its consistence. Encephaloid and scirrhus cannot be regarded as in any way constituting distinct varieties of carcinoma. There are all intermediate stages between them, and the differences in the rapidity of their growth, and consequently in thier structure and physical characters, constitute their only distinctive features.

The epithelial growth in encephaloid is rapid and abundant, and the cells, for the most part larger than in scirrhus, quickly undergo fatty degeneration, so that often more free nuclei than cells are visible.

The proportion of stroma is very small, and owing to the rapidity of its growth, it is much less fibrous than that of scirrhus, and does not undergo a similar cicatricial contraction. (Fig. 57.) The bloodvessels are often very abundant, and the tissue supporting them being soft and non-resistant, hemorrhage occasionally takes place.

Encephaloid cancer is of a soft brain-like consistence, the central portions, where fatty degeneration is most advanced, often being com-

FIG. 57.



Encephaloid Cancer.—From a secondary cancer of the liver, showing the large size of the alveoli and the thinness of their walls. In the latter, small cells are visible. The large epithelial cells are commencing to undergo fatty metamorphosis. $\times 200$.

pletely diffuent. The tumor is sometimes more or less lobulated. On section, it presents a white pulpy mass, much resembling brain-substance, which is often irregularly stained with extravasated blood.

Encephaloid is much less common than scirrhus cancer. It is most frequently met with in internal organs as a *secondary* growth. It also sometimes occurs primarily in the testis and mamma. Many growths formerly described as encephaloid cancer, are soft sarcomata. (See “Round-celled Sarcoma.”)

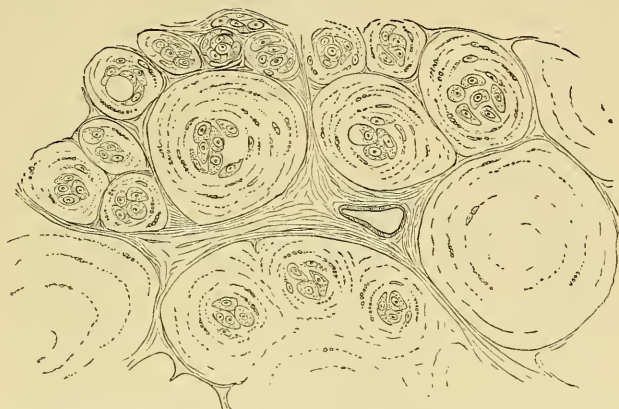
Colloid Cancer.

The growths described under the name of *colloid*, *alveolar*, or *gelatiniform* cancer, although sometimes regarded as constituting a distinct variety of cancer, are simply one of the preceding forms which have undergone a mucoid or colloid change. The frequency with which non-cancerous growths which have undergone these forms of degeneration have been confounded with colloid cancer, has already been alluded to. (See “Colloid Degeneration.”)

The alveolar structure in colloid cancers is very marked. The alveoli have very thin walls; they are large, distinct, and more or less spherical in shape. This large size and distinctness of the alveoli is owing to their distension with the softened substance. Within them is contained the gelatinous colloid material, which is a glistening, translucent, colorless, or yellowish substance, of the consistence of thin mucilage or size-gelatin. In the main it is perfectly structureless; within it, however, are embedded a varying number of epithelial cells, which also contain the same gelatinous substance. (Fig. 58.) These cells present a peculiar appearance: they are large and spherical in shape, and are distended with drops of the same gelatinous material as that in which they are embedded. (See Fig. 58.) Many of them display a lamellar surface, their boundary being marked by concentric lines. It would appear that the colloid change commences in the cells, which become gradually destroyed in the process. In

other cases the cells, with the exception of slight fatty metamorphosis, are but little affected, and the substance distending the alveoli is more

FIG. 58.



Colloid Cancer.—Showing the large alveoli, within which is contained the gelatinous colloid material. $\times 300$. (Rindfleisch.)

viscid and mucoid in character. This is due to a mucoid degeneration of the intercellular substance, rather than to a colloid change commencing in the cells. (See “Mucoid Degeneration.”)

Colloid cancer is most frequently met with in the stomach, in the intestine, in the omentum, and in the peritoneum.

Epithelioma.

Epithelioma, or *epithelial cancer*, must be regarded as constituting a much more distinct variety of carcinoma than either of the preceding, although transitional forms between it and scirrhus are occasionally met with. It differs from the other varieties of cancer in always growing in connection with a cutaneous or mucous surface—the junction of the two being its usual seat—and in its epithelial elements closely resembling the squamous variety of epithelium.

The cells of epithelioma are in the main indistinguishable from those met with on the cutaneous surfaces, and on the mucous membrane of the mouth. They vary in size from $\frac{1}{300}$ to $\frac{1}{1000}$ th of an inch in diameter, the average being $\frac{1}{700}$ th. They contain usually a single nucleus; frequently, however, the nuclei are multiple. (Fig. 59.) They are often considerably flattened and distorted in shape, owing to the pressure to which in their growth they are subjected, but they

never present those numerous varieties in outline which are met with in the other varieties of carcinoma, neither do they exhibit the same marked tendency to undergo fatty degeneration. The arrangement

FIG. 59.

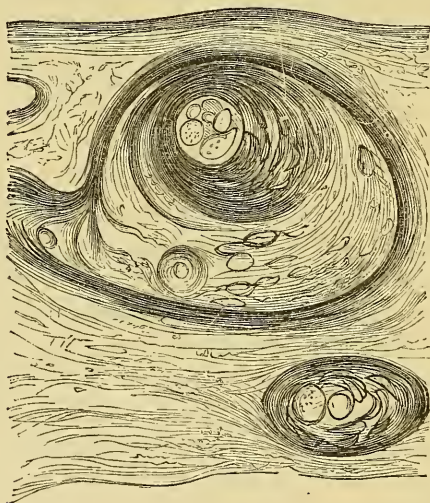


Cells from an Epithelioma of the Lip. $\times 250$.

of these cells is peculiar: some of them are situated in irregular tubular-shaped lobules which communicate with each other; others are less regularly grouped in masses of various sizes amongst the meshes of a stroma. As the cells increase in number they tend to become arranged concentrically in groups so as to form globular masses. These masses are the "concentric globes," or "epithelial nests," which are so commonly met with wherever squamous epithelium is undergoing rapid growth, and which, although not distinctive,

are exceedingly characteristic of epithelioma. As the epithelium multiplies, the peripheral layers of cells become flattened by pressure

FIG. 60.

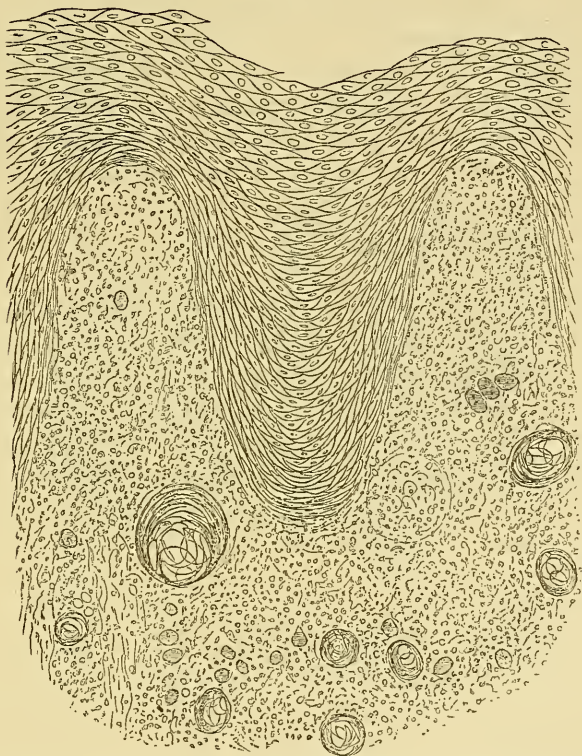


Epithelioma of the Lip.—Showing the concentric globes of epithelial cells. $\times 100$.

against the surrounding structures, whilst those in the centre remain more or less spherical in shape like those of the deeper layers of the epidermis. (Fig. 60.) The cells may be so closely packed as ultimately

to become hard and dry like those of the nails and hair, and the globes are then of a brownish-yellow color and of a firm consistence. The globes are often large enough to be readily visible to the naked eye, and owing to the arrangement of the epidermic scales, they usually present a fibrous appearance.

FIG. 61.



Epithelioma of the Tongue.—A thin vertical section, showing the excessive epithelial growth upon the surface of the papillæ, and the extension of the epithelial elements into the subjacent connective tissue. The sub-epithelial tissue is infiltrated with small ("indifferent") cells, amongst which are seen the epithelial elements both single and forming concentric globes. $\times 100$.

The stroma presents every variation between rapidly growing embryonic, and an incompletely fibrillated tissue. It may be tolerably abundant, or almost entirely wanting. It rarely forms such a marked alveolar structure as that which characterizes the other varieties of carcinoma, but usually consists simply of a small-celled infiltration surrounding the epithelial elements, which may ultimately become developed into a more or less completely fibrillated tissue. (Fig. 61.)

With regard to the development of epithelioma—this is much more frequently determined by some external source of irritation than is that of the other varieties of carcinoma. The epithelial elements are undoubtedly derived from the epithelium of the skin or mucous membranes, or from that of the glands which are situated in these tissues. The growth commences by a proliferation of this epithelium, which, as it increases, becomes *heterologous*, extending beyond the normal limits into the subjacent connective tissue, and even into muscle, bone, and other structures (Fig. 61); and it is this heterologous development of epithelium which is the essential characteristic of epithelioma. The extension of the epithelium into the subjacent connective tissue produces in the latter an irritative growth, and thus the groups of epithelial elements are always surrounded by a small-celled (“indifferent”) tissue, the small-celled growth preceding the epithelial invasion. (Fig. 61.)

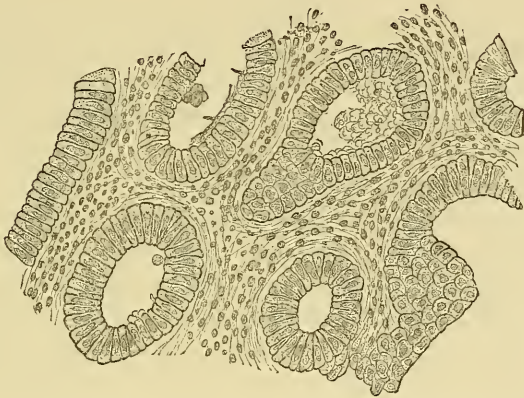
Epithelioma usually presents itself in the first place either as a small foul ulcer with indurated edges, or as a subcutaneous induration or nodule which subsequently ulcerates. The surface of the ulcer is frequently papillated and villous, owing to the irregular growth of the corium. The tumor itself is firm in consistence, often more or less friable, and on section presents a grayish-white granular surface, sometimes intersected with lines of fibrous tissue. The cut-surface yields on pressure a small quantity of turbid liquid, and in many cases also a peculiar, thick, crumbling, curdy material, can be expressed, which often comes out in a worm-like shape, like the sebaceous matter from the glands of the skin. This latter is very characteristic. It is composed of epithelial scales, and on being mixed with water it does not diffuse itself like the juice of other cancers, but separates into minute visible particles. If it is very abundant, the cancer is soft and friable, and the material can be seen in the cut-surface as small scattered opaque dots.

Epithelioma has its primary seat in the immediate vicinity of the cutaneous or mucous surfaces, the point of junction of the two being its favorite habitat. It appears in most cases, as already stated, to owe its origin to some external source of irritation. It is rare in the young, and is most frequently met with in the lower lip at the junction of the skin and mucous membrane, on the tongue, prepuce, scrotum (“chimney-sweep’s cancer”) labia, eyelids, cheeks, and in the uterus and bladder. As it extends it may involve any tissue—muscle,

bone, and tendon may be alike implicated. It usually infects the lymphatic glands, but very rarely occurs in internal organs.

Cylindrical Epithelioma, or Adenoid Cancer.—These terms are applied to those forms of epithelial cancer which grow from mucous membranes with columnar (cylindrical) epithelium, as from those of the stomach and intestines. In these tumors the epithelial elements are similar to those of the mucous membrane from which they grow. They are cylindrical in shape, and are arranged perpendicularly to the walls of the alveoli in a manner precisely analogous to that of the columnar epithelium on the mucous surface. (Fig. 62.) There is

FIG. 62.



Cylindrical Epithelioma.—From the colon. $\times 200$ reduced $\frac{1}{2}$.

rarely a formation of concentric globes, and the growths are of a soft, and often gelatinous consistence. These tumors cause secondary growths in the lymphatic glands, and sometimes in the liver, lungs, and bones, which possess the same characters as the primary cancer. The distinction between them and simple adenomata is often exceedingly difficult. (See “Adenoma of Mucous Membranes.”)

CLINICAL CHARACTERS OF THE CARCINOMATA.—In speaking of the clinical characters of the cancers, it is important in the first place to make a distinction between epithelioma and the other varieties. Epithelioma, as far as its malignancy is concerned, occupies a very inferior position to scirrhus, encephaloid, and colloid. These latter varieties of carcinoma possess in the highest degree malignant properties. They extend locally, invading indiscriminately the tissues

amongst which they grow, and reproduce themselves in the lymphatic glands and in internal organs. In the process of dissemination, however, they present some peculiarities which distinguish them from growths which are sometimes equally malignant—viz., the sarcomata. The carcinomata are characterized by their great tendency to reproduce themselves in the neighboring lymphatic glands. This implication of the lymphatics is usually much more marked than in the sarcomata, in which it but comparatively rarely occurs, and this is probably owing to the communication of the lymphatic vessels with the alveolar spaces of the cancerous growth. The general dissemination in internal organs, on the other hand, is often effected much less readily in carcinoma than in sarcoma, and the course of the former is therefore sometimes more protracted than that of the latter. This difference is explained by the difference in the distribution of the bloodvessels:—in carcinoma, these are contained in the stroma, and very rarely come into contact with the cells of the growth; whereas in the sarcomata, they ramify amongst the cells, and their walls being composed of thin embryonic tissue like that of the growth which they supply, dissemination through the medium of the blood is rapidly and readily effected. In carcinoma, the lymph being so important a medium of infection, the reproduction of the growths in internal organs may be considerably delayed: the progress of the disease becomes arrested by the lymphatic glands, and its further dissemination is often only effected after these have become very generally and extensively involved.

With regard to the difference in the clinical characters of these three varieties of carcinoma—the dissemination of encephaloid takes place much more rapidly than that of scirrhus, owing to the greater rapidity of its growth, its greater vascularity, and the greater activity of its epithelial elements. Colloid is somewhat inferior in the degree of its malignancy to both scirrhus and encephaloid.

Epithelioma is of all the cancers much the least malignant. It extends locally, and may infect the neighboring lymphatics, but it comparatively rarely reproduces itself in internal organs. This is probably owing to the size and character of its epithelial elements, which render them much less liable to be transmitted by the blood and lymph-streams than are the cells of the other varieties of cancer.

In all the varieties of carcinoma there is a tendency for the secondary growths to repeat the characters of the primary one. This is most marked in epithelioma. In scirrhus, the secondary growths in internal

organs, although sometimes resembling the primary tumor, are often more rapidly developed, are softer and more vascular, and in accordance with the distinction which has been made between scirrhus and encephaloid, they must be regarded as belonging to the latter variety of cancer.

CHAPTER XXIV.

CYSTS.

IN addition to the new growths already described, there is a large class of formations, many of which cannot be regarded as "tumors" in the strict application of this term. These are the *cysts* or *cystic tumors*.

A *cyst* is a cavity containing liquid or pultaceous material, which is separated from the surrounding structures by a more or less distinct capsule. It may be a new formation, or a pre-existing structure which has become distended by its own secretion, or by extravasation into it. The former, only, comes within the category of new growths, although, for the sake of convenience, it will be advisable to consider them both under one head.

There are thus two principal modes by which cysts originate—one, the most frequent, by the gradual accumulation of substances within the cavities of pre-existing structures, which are, for the most part, products of their own formation, being in some cases a secretion, and in others a cell-growth; the other, by the independent formation of a cyst in the tissues.

The accumulation of secretions and of other products within pre-existing cavities, may be effected in the three following ways:—

1st. By the retention of the normal secretion owing to the closure of the excretory ducts—as so often occurs in sebaceous glands.

2d. By excessive secretion, the cavity being unprovided with an excretory duct—as in the formation of bursæ.

3d. By the extravasation of blood into the cavity—as in hæmatocele.

The independent formation of a cyst may take place—

1st. By the softening and liquefaction of the tissues in some par-

ticular part, owing to mucoid or fatty changes. The tissues around the softened matters become condensed, and ultimately form a kind of cyst-wall.

2d. By the enlargement and fusion of the spaces in connective tissue, and the accumulation of fluids within them. The surrounding tissue becomes condensed, and forms a cyst wall; and this may, in some cases, become lined with secreting cells.

3d. By the formation of a cyst-wall around foreign bodies, parasites, or extravasated blood.

STRUCTURE.—The wall of the cyst will vary in its nature according as it is a pre-existing or a newly-formed tissue. In the former case, it will possess an epithelial lining which will present the same characters as that of the gland, serous membrane, or other structure, from which the cyst originated. If the cyst is a new growth, it rarely possesses an epithelial lining, but consists simply of a fibrous capsule. The cyst-wall is sometimes firmly connected with the adjacent parts, so that it can only with difficulty be separated; in other cases, the union is much less intimate. Instead of being a distinct structure, it may be simply the surrounding tissue which has become dense and fibrous in character.

The contents of cysts are very various, and may serve as a basis for their classification. In the retention-cysts, they will vary with the nature of the normal secretion—serum, sebaceous matter, saliva, milk, seminal fluid, and other substances are thus found in these cysts, more or less altered in character from being retained in a closed cavity. In the exudation-cysts, serum is the most frequent constituent; and in extravasation-cysts, blood. In those cysts which originate from the softening and breaking down of tissue, the contents are the products of retrogressive tissue-metamorphosis, and usually consist largely of mucin, fatty matters, and serum.

SECONDARY CHANGES.—These may take place in the wall of the cyst or in its contents. The cyst-wall itself may become the seat of new growths, and produce secondary cysts, villous, glandular, and other structures:—this occurs in many compound ovarian cysts. It may also be the seat of an inflammatory process, which terminates in suppuration and granulation, and by this means the cyst frequently becomes obliterated, its contents being either absorbed or discharged externally, and the cavity closing by granulation. Calcification and ossification of the wall may also occur. The contents of cysts undergo various changes, owing to their retention in a closed cavity. The

secretions become altered in character, thickened, and viscid. Epithelial elements undergo fatty changes, and so give rise to cholesterolin crystals. Calcification of the contents is also common.

Cysts may be *simple* or *compound*. A simple cyst consists of a single loculus. A compound or multilocular cyst is one consisting of numerous loculi, which either communicate with one another or remain isolated. Another variety of compound cyst consists of a cyst with endogenous growths, the larger cyst having others growing from its walls. A compound cyst may become a simple one by the destruction of its walls.

Cysts are frequently associated with other growths, hence the terms—"cystic-sarcoma," "cystic-cancer," etc. It is especially in those growths which originate in glandular structures, as in the mamma, testicle, and ovary, that this combination is met with. The cystic development may almost entirely obliterate the structure of the tumor in which it takes place, so that ultimately the latter becomes converted into a combination of cysts. In other cases large portions of the tumor grow into the cystic cavities. Considerable difficulty is thus not unfrequently caused in determining the nature of the original growth.

CLASSIFICATION.—Cysts may be most conveniently classified according to their mode of origin, thus :—

CLASSIFICATION OF CYSTS.

- I. *Cysts formed by the accumulation of substances within the cavities of pre-existing structures.*
 - A. RETENTION CYSTS.—Cysts resulting from the retention of normal secretions. These include—
 - α. *Sebaceous Cysts*.—These are formed by the retention of secretions in the sebaceous glands. Such are comedones and atheromatous tumors.
 - β. *Mucous Cysts*.—These are formed by the retention of secretions in the glands of mucous membranes.
 - γ. *Cysts from the retention of secretions in other parts*, including—Ranula, from occlusion of the salivary ducts ; Encysted Hydrocele, from occlusion of the tubuli testis ; cysts in the mammary gland, from obstruction of the lacteal ducts ; simple and some compound cysts of the ovary, from dilatation of the Graafian follicles ; and simple cysts of the liver and kidneys.

- B. EXUDATION CYSTS.—Cysts resulting from excessive secretion in cavities unprovided with an excretory duct. These include Bursæ, Ganglia, Hydrocele, and many cysts in the broad ligament.
- C. EXTRAVASATION CYSTS.—Cysts resulting from extravasation into closed cavities. These include Hæmatocele, and some other forms of sanguineous cysts.
- II. *Cysts of independent origin.*
- A. CYSTS FROM SOFTENING OF TISSUES.—These are especially common in new formations, as in enchondroma, lipoma, sarcoma, etc.
- B. CYSTS FROM EXPANSION AND FUSION OF SPACES IN CONNECTIVE TISSUE.—These include—
- a. *Bursæ*, originating from irritation and exudation into the tissues.
 - β. *Serous cysts in the neck* (often congenital).
 - γ. *Many compound ovarian cysts*.¹
- C. CYSTS FORMED AROUND FOREIGN BODIES, EXTRAVASATED BLOOD, AND PARASITES.
- D. CONGENITAL CYSTS.—These include many Dermoid cysts. These appear often to be the remains of blighted ova. They contain fatty matters, hair, teeth, bones, etc.

CHAPTER XXV.

CHANGES IN THE BLOOD AND CIRCULATION.

Local Anæmia.

LOCAL anæmia, or ischæmia, is diminution of blood in a part owing to diminished arterial supply.

CAUSES.—The most frequent causes of diminished arterial supply are all those conditions which either narrow or completely close the

¹ See Dr. Wilson Fox, on Cystic Tumors of the Ovary: *Med. Chir. Soc. Trans.*, vol. xlvii.

lumen of the artery. The lumen of an artery may be diminished by disease of its walls—atheroma, calcification, and syphilis; or by pressure exercised upon it from without, as by new growths, inflammatory exudations, and mechanical or inflammatory effusions. The complete closure of the vessel may result from some of the foregoing conditions, or more commonly from thrombosis, embolism, or ligature. In some cases the supply of blood is diminished by an increase in the natural resistance of the artery from irritation of the vaso-motor nerve. This occurs as the result of a low temperature, in some neuralgic and other nervous affections, and from the action of certain substances, such as ergot of rye, opium, etc.

RESULTS.—A part with diminished arterial supply is usually paler, less tense, and of a lower temperature than natural. Its nutrition and function are also impaired, so that it may atrophy, undergo fatty degeneration, or die. These results were exemplified in the chapters on atrophy, fatty degeneration, and necrosis.

The results of diminished arterial supply, however, will obviously depend upon the extent of the diminution. Where there is any obstruction of the main artery or arteries leading to a part, there is increased pressure in the vessels behind the obstruction, and in many cases the anatomical distribution of these is such that they gradually restore the circulation in the anæmic area. This restitution may be effected before the nutrition of the part has time to suffer. In certain tissues, however, the bloodvessels are so arranged that when an artery is obstructed the circulation cannot thus be restored by collateral branches. The obstruction of the artery is then followed in the first place by complete anæmia of a certain area, but the blood-pressure from behind being annihilated, there is a backward pressure from the veins, and if these contain no valves, the venous blood regurgitates, and so again fills the capillaries. (Cohnheim.) Such arteries, with which anastomoses do not exist, are termed by Cohnheim "terminal" arteries. They occur in the spleen, kidneys, lungs, brain, and retina; and obstructions in these tissues are necessarily followed by much greater nutritive disturbance than in those in which there is a free arterial anastomosis.

Important changes also take place in the walls of the bloodvessels as the result of deprivation of arterial blood. These changes have been studied experimentally by Cohnheim, and may be thus briefly summarized: If the ear of a rabbit be ligatured at its root, and the ligature, after remaining on for from eight to ten hours, be removed

and the blood again allowed to circulate, the organ becomes exceedingly vascular, red, swollen, and oedematous; and when examined microscopically the vessels are found to be dilated, and numerous white blood-corpuscles to have escaped from them into the surrounding tissue. The longer the circulation has been obstructed the more abundant is the infiltration with leucocytes, and when the obstruction has lasted for twenty-four hours small extravasations of blood also occur. If the ligature be allowed to remain on for forty-eight hours the ear dies. From these observations Cohnheim concludes—that when bloodvessels with their vasa vasorum are deprived of their circulating blood for a sufficient length of time they lose their power of retaining the blood, and so allow the liquor sanguinis and white blood-corpuscles to escape from them, the escape taking place principally through the capillaries and veins. In order, however, for the walls of the bloodvessels to be thus altered, the interference with the circulation must be very complete—a very little vascular supply serves to maintain their nutrition. These changes, as will be seen subsequently, explain that hemorrhagic infarction which results from the blocking of a terminal artery. (See “Embolism.”)

Hyperæmia.

Hyperæmia, or congestion, is excess of blood in the more or less dilated vessels of a part. Whatever increases the pressure of the blood, or diminishes the resistance of the vessels, may be a cause of hyperæmia. Hyperæmia is *active* or *arterial*, and *mechanical* or *venous*. These two varieties must be considered separately.

Active Hyperæmia.

Active hyperæmia is an excess of blood in the arteries of a part, with, in most cases, an acceleration of the flow.

CAUSES.—The causes of active hyperæmia may be divided into those which increase blood-pressure, and those which diminish arterial resistance.

1. *Increased Blood-pressure*.—This occurs most commonly from interruption of the main current of blood in any particular part, owing to which increased pressure is thrown upon the collateral vessels. These vessels thus become dilated, the amount of blood in them

is increased, and the flow is accelerated. This, which is known as *collateral hyperæmia*, is seen after the obstruction of the main current from any cause, as from the ligature of the vessel, or from its occlusion by a thrombus or embolus. (See "Embolism.")

General obstruction in the capillaries of a part will in the same way cause a compensatory hyperæmia. This is exemplified by the application of external cold, causing contraction of the superficial capillaries and congestion of internal organs; and by obstruction of the capillaries in one part of an organ causing hyperæmia of the parts adjacent.

2. *Diminished Arterial Resistance*.—This is much the most frequent cause of active hyperæmia. It may arise from—

a. *Relaxation or paralysis of the wall of the vessel*.—The relaxation of the muscular coat of the vessels and their consequent dilatation, may be owing to—1st, external warmth; 2d, direct paralysis of the vaso-motor nerve; 3d, indirect paralysis of the vaso-motor nerve; and 4th, changes in the walls of the vessel resulting from injury independently of the nervous centres. External warmth is a common cause of hyperæmia. This is seen in the effect of warm baths, fomentations, etc.

The effects of direct paralysis of the vaso-motor nerves are seen in the active congestion of the head and neck which follows pressure upon the sympathetic in the neck, as by an aneurism; and in the unilateral congestion which results from experimental sections or disease of one-half of the spinal cord. Some emotional conditions also are attended by paralysis of the vascular nerves and consequently by active hyperæmia; this is seen in blushing. Certain substances, again, taken internally, produce vaso-motor paralysis, as the nitrite of amyl, alcohol, tobacco, etc.

Indirect or reflex paralysis of the vaso-motor nerves is most frequently due to irritation of sensory nerves. The dilating action of the irritated sensory nerve is usually confined to the region supplied by it. Of the numerous examples of hyperæmia from this cause, may be mentioned that which follows injury of the conjunctiva, the hyperæmias associated with facial neuralgias, and the priapism that often results from irritation of the urethra. The hyperæmia of the skin, caused by friction and irritating substances, is also due to the same cause.

Hyperæmia from the direct injury of the walls of the vessel independently of the nervous system occurs as the earliest change in the

process of inflammation. In inflammation, the irritation is so severe as to cause not only dilatation of the vessel and accelerated blood-flow, but also a subsequent retardation of the circulation and exudation of liquor sanguinis and blood-corpuscles. (See "Inflammation.") If the injury be less intense or less prolonged in its action, it produces simply dilatation of the vessels and increased rapidity of flow—*i. e.* active hyperæmia.

β. *Sudden removal of external pressure.*—The sudden removal of external pressure from vessels is followed by their dilatation, and consequently by hyperæmia. As examples of hyperæmia from this cause, may be mentioned that which results from the sudden removal of ascitic fluid, and the fluid from a hydrocele.

The removal of atmospheric pressure from a part such as is done by dry cupping, although often included under this head, really produces quite a different result. Here not only the arteries are involved, but also the veins and capillaries, so that the part fills with blood both from the arterial and venous sides of the circulation. The blood-flow also instead of being accelerated is retarded, and there is often complete stasis.

γ. *Atony of the walls of the vessels from mal-nutrition.*—This is a much less important cause of hyperæmia. Fatty degeneration of the muscular and internal coats of the smaller arteries may, however, in some cases lead to their dilatation, and thus be a cause of active hyperæmia.

RESULTS.—The results of active hyperæmia are principally such as might be expected to follow from an increase in the amount of the arterial blood, and in the rapidity of its flow, in any particular organ or tissue. There is increased redness and pulsation, a sensation of throbbing being often experienced by the patient. There is also some increase in bulk. The temperature at the same time undergoes a marked elevation, sometimes as much as 3° Cent. If the hyperæmia be of long duration the small arteries become permanently enlarged, their walls gradually thicken, and the peri-vascular connective tissue may increase. Hypertrophy of other tissues is also a frequent result. (See "Increased Nutrition" and "Hypertrophy.") Function may, or may not be interfered with. It is in the nervous centres that functional changes are most marked. They include great excitability, paræsthesiæ of sight and hearing, convulsions, etc. In the skin, kidneys, and other secreting organs, the secretions are usually increased.

Mechanical Hyperæmia.

In mechanical hyperæmia, the excess of blood is principally in the veins, and the flow, instead of being accelerated, is retarded.

CAUSES.—The causes of mechanical hyperæmia are such as interfere with the return of the blood by the veins, either by directly impeding its exit from any vein or system of veins, or by diminishing the normal circulating forces. They are—

1. *A direct Impediment to the Return of Blood by the Veins.*—This is the most fertile cause of mechanical hyperæmia. Any obstruction to the return of blood by the veins is followed by distension and impeded flow behind the obstruction. The congestion of some of the abdominal viscera which results from the obstruction to the portal circulation in cirrhosis of the liver; that of the lung in mitral constriction and regurgitation; that of the systemic circulation in insufficiency of the tricuspid valve; and that of the lower extremities from the pressure of the gravid uterus on the iliac veins, are a few of the numerous familiar examples of mechanical hyperæmia from this cause.

2. *Diminished Cardiac Power.*—This is one of the most important causes of mechanical hyperæmia. The motor power of the heart becomes impaired in many of the chronic exhausting diseases, also in the acute febrile diseases, as in typhus and typhoid fever, and in all those conditions of degeneration of its structure which lead to the dilatation of its cavities. In whichever of these ways the *vis a tergo* is diminished, it will tend to produce that diminished fulness of the arteries and over-fulness of the veins which is so familiar clinically as the result of cardiac failure. Not only so, but if the condition be of long duration, there is necessarily so much interference with the changes of the blood in the lungs, with the function of the blood-forming organs, and with the processes of digestion and assimilation, that the blood itself becomes deteriorated, and thus the nutrition of the tissues generally suffers.

3. *Gravitation.*—This becomes an important auxiliary in the production of hyperæmia in disease, especially when it is associated with diminished cardiac power. The effect of gravitation in determining congestion of the most dependent parts is exemplified in chronic exhaustive and in many of the acute febrile diseases, in which the nutrition generally becomes impaired, the heart's power weakened, and in which the patient, confined to bed, is unable frequently to

change his position. The integuments of the back, and the posterior portions of the lungs, are the parts which are thus most frequently affected. (Hypostatic Congestion.) Gravitation in the same way determines the initial swelling of the legs in cases of cardiac dropsy.

4. *Increased Local Resistance.*—This results from diseased conditions of the arterial walls, owing to which they either lose their elasticity and contractility and thus their power of equalizing and regulating the blood-flow, or become considerably enlarged. In either case the circulation will be impeded, there will be an accumulation of blood and retardation of flow in the veins beyond, and the veins themselves will gradually become relaxed and dilated. Such conditions may arise from simple atony of the arterial walls, or from atheromatous, fatty, or calcareous changes. They are most common in advanced life. The part they play in the production of senile gangrene has been already alluded to. (See “Senile Gangrene.”)

RESULTS.—Whether there be a direct impediment to the return of blood by the veins or a failure in the circulating forces, the veins and capillaries dilate, and the blood accumulates in them and moves with diminished velocity. The subsequent changes will depend upon the amount of obstruction to the venous return and the force of the arterial circulation; in other words, upon the amount of pressure and the relation of the pressure in the arteries to that in the veins. The most important of these changes are *the transudation of serum, the diapedesis of the red blood-corpuscles, hemorrhage, fibroid induration, thrombosis, and necrosis.*

1. *Transudation of Serum.*—This, which is one of the most important results of mechanical hyperæmia, is due to the difference in the amount of blood-flow to and from the part. Hence, the greater the impediment to the return by the veins, and the greater the arterial supply, the greater the tendency to transudation. The influence of the arterial supply upon the amount of transudation is shown experimentally by producing dilatation of the arteries by section of their vaso-motor nerves. If in the rabbit the main vein of the ear be ligatured on both sides, and the sympathetic be divided in the neck on one side, the transudation of serum into the ear of that side on which the nerve was divided will be very considerable, whilst on the other side it will be slight, or entirely wanting. The serum transudes mainly from the capillaries and small veins, and not from the small arteries. It differs from blood-serum in being of lower specific gravity, and in containing more water and less of the solid constituents.

The greater the pressure, the more nearly does the transuded liquid resemble the liquor sanguinis, and the greater is the amount of albumen which it contains. If the pressure be very great it may yield a fibrinous coagulum.

This augmented transudation from the bloodvessels causes an increase in the absorption by the lymphatics, and this increase may be sufficient to prevent any accumulation of serum in the part—as is the case, for example, in the ear of the rabbit, where the main vein is obliterated but the arteries are not dilated (see *antea*). Where the lymphatic absorption, however, is insufficient to remove the transuded liquid, this accumulates and gives rise to *œdema* and dropsical effusion. The amount of transudation will be influenced by the anatomical characters of the tissue, being most in those parts in which the bloodvessels are least supported, as in the subcutaneous tissue, and in tissues which present a free surface, as serous and mucous membranes. A lax and toneless condition of the vessels will also favor transudation.

2. *Diapedesis of Red Blood-corpuscles*.—When the obstruction to the venous return is very great, not only does serum transude from the veins and capillaries, but some of the red blood-corpuscles also escape from the same vessels. This diapedesis of the red corpuscles in conditions of mechanical hyperæmia was discovered by Cohnheim. It may be observed in the web or tongue of the frog after ligature of the main vein. The red corpuscles accumulate in increasing numbers in the veins and capillaries, the blood-stream in these vessels completely stagnates, the red corpuscles become so closely packed that their individual outlines are scarcely distinguishable, the coherent mass oscillates to and fro with the arterial pulsation, and then suddenly some of the red corpuscles penetrate the walls of the small veins and capillaries and escape into the surrounding tissue. This diapedesis occurs without rupture of the vessel, and if the ligature be removed, the blood again circulates in a perfectly normal manner. The corpuscles appear to be squeezed through the capillary walls as the result of the pressure. They rarely escape in great numbers, and they possibly do so by passing through the stomata which Recklinghausen has shown to exist between the endothelial elements; although Cohnheim considers that the existence of these is not necessary to account for the diapedesis.

3. *Hemorrhage*.—This is another result of mechanical hyperæmia. It usually occurs only when the obstruction to the venous current is very great. Those vessels which are the least supported are the

first to give way. The hemorrhage into the stomach in cirrhosis of the liver, and into the lung in mitral disease, are familiar examples of hemorrhage from this cause.

4. *Fibroid Induration*.—This, which is due to a gradual increase in the connective tissue around the bloodvessels, is one of the most important results of long continued mechanical hyperæmia. The interstitial growth leads to atrophy of the other structures, and thus to impairment of the functions of the organ. In the stomach, it produces atrophy of the glandular structures; in the kidney, compression of the urine tubes; in the liver, obstruction to the portal circulation; in the heart, diminution in motor power. The alterations which this change produces in the physical characters of the organs—viz., a hardness and induration associated with abnormal redness or pigmentation due to the excess of blood, are exceedingly characteristic.

5. *Thrombosis*.—This, as a result of mechanical obstruction, will be described in the following chapter.

6. *Necrosis*.—This only occurs from mechanical hyperæmia when the obstruction is very general and complete. It has been already described under the head of “Necrosis.”

In addition to the foregoing, long-continued mechanical hyperæmia leads to impairment of vitality and function. The tissues gradually atrophy and undergo retrogressive changes, although from the amount of serosity and blood which they contain, their size and absolute weight may be increased. Their temperature becomes lowered. This form of hyperæmia has no tendency to cause hypertrophy. In mucous membranes it gives rise to catarrh.

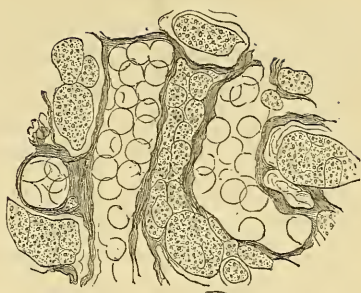
MECHANICAL HYPERÆMIA OF THE LIVER.—NUTMEG LIVER.—Long-continued mechanical hyperæmia of the liver gives rise to the condition known as *Nutmeg Liver*. This is the condition which so frequently results from disease of the heart. The change is characterized by a large accumulation of blood in the hepatic veins, by dilatation and thickening of the veins, by atrophy of the hepatic cells in the central portions of the acini, and by an increase in the interlobular connective tissue. The impediment to the return of blood by the hepatic vein leads to atrophy of the cells in the central portions of the acini and also to the formation of granular pigment, so that when examined microscopically, these portions of the acini are seen to consist of broken-down cells and granules of pigment. (Fig. 63.) The veins here are found much dilated, and filled with red blood-corpuscles. (Fig. 64.) Their walls are thickened, and there often

FIG. 63.



Nutmeg Liver.—Showing the destruction of the liver-cells and the pigmentation of the central portions of the acinus, together with the new growth of connective tissue at the periphery. V. Hepatic vein. P. Portal canal. $\times 50$. (When the specimen is more highly magnified, the peripheral connective tissue growth is seen to contain numerous nuclei.)

FIG. 64.



Nutmeg Liver.—Portion of Fig. 63, around central hepatic vein (V), more highly magnified. Showing the thickening of the veins, and the accumulation of red blood-corpuscles within them. $\times 400$.

appears to be also more or less thickening of the intercellular network which immediately surrounds the central vein. Owing to this thickening of the central vein and of the adjacent intercellular network, and to the destruction of the liver-cells, the

most central portions of the acini, in advanced stages of the disease, may present a fibrous appearance. At the peripheral parts of the acini the new interlobular growth is seen insinuating itself between the almost unaltered liver cells. This new interlobular growth is usually distinctly nucleated, but, for the most part, less so than that met with in cirrhosis. Its cellular character has been especially insisted upon by Dr. Wickham Legg.

In the earlier stages of this affection the liver is often considerably increased in size from the large amount of blood which it contains. On section, it presents a peculiar mottled appearance, the centre of the lobules being of a dark red color, whilst the peripheral portions are of a yellowish-white. This latter appearance is often increased by the presence of more or less fat in the peripheral liver-cells. Ultimately the organ may undergo a gradual diminution in size. This is due partly to the atrophy of the cells in the central portions of the lobule, and partly to the pressure of the interlobular growth. The interlobular growth tends to cause obstruction to the portal circulation, as in cirrhosis.

MECHANICAL HYPERÆMIA OF THE LUNGS.—In the lungs, long-continued mechanical hyperæmia produces that peculiar induration and pigmentation of the organs which is known as *Brown Induration*. This condition most frequently results from stenosis and insufficiency of the mitral orifice. The alterations produced in the pulmonary texture consist in the first place of elongation and dilatation of the pulmonary capillaries, so that even in uninjected preparations the alveolar walls appear abnormally tortuous. The epithelial cells lining the alveoli also become swollen and probably multiply, and they are seen in large numbers, filled with dark brown pigment, covering the alveolar walls. (Fig. 65.) They frequently accumulate within the

FIG. 65.



Brown Induration of the Lung.—Showing the abnormal number of swollen pigmented epithelial cells covering the alveolar walls, the increase of connective tissue around the bloodvessels, *a*, and the large quantity of pigment. *b*. The alveolar cavity. $\times 200$.

alveolar cavities. These changes are followed by an increase in the interlobular connective tissue, by the formation of large quantities of brownish-black pigment, and often by a thickening of the alveolar walls. Sometimes the pulmonary capillaries rupture, and blood is extravasated into the lung-tissue.

Lungs in which these changes are at all advanced present a more or less uniform brownish-red tint, mottled with brown or blackish-colored specks and streaks. They are heavier and tougher than natural, less crepitant, and upon squeezing them the pulmonary tissue is found to be denser and thicker than that of a healthy lung.

POST-MORTEM APPEARANCES OF HYPERÆMIA.—The post-mortem appearances presented by hyperæmic organs and tissues vary con-

siderably. Very frequently parts which were hyperæmic during life show no signs of it after death. If the blood does not coagulate rapidly it passes on into the veins, and thus the recognition of arterial and capillary hyperæmia very often becomes impossible. The effect of gravitation must also be taken into account in estimating hyperæmia. After death the blood naturally gravitates to the most dependent parts:—this is seen in the post-mortem congestion of the posterior portions of the lungs, and of the most dependent portions of the various coils of the intestine. The uniform redness of post-mortem staining again, must not be confounded with the redness of hyperæmia. In capillary and arterial hyperæmia, the color is red, and the injection often presents the appearance of a capilliform network. If very intense it may to the naked eye appear uniform, but a lens will always discover its capillary nature. When the veins are the seat of the hyperæmia the injection is called ramiform, and the color is dark blue.

The anatomical peculiarities in the distribution of the bloodvessels will, however, materially affect the appearance of the hyperæmia. In the intestines it is often punctiform, being situated in the vessels of the villi; so also in the kidney, when its seat is the Malpighian corpuscles. A punctiform appearance may also be produced by minute extravasations of blood. If the hyperæmia is of long standing, the tissue becomes pigmented. This is often well seen in the stomach and intestines, also in the lungs.

CHAPTER XXVI.

THROMBOSIS.

THROMBOSIS is a coagulation of the blood within the vessels during life. The coagulum is called a *thrombus*. It may form in the heart, in the arteries, in the capillaries, or in the veins. It is much the most common in the last-named vessels.

CAUSES.—The phenomenon of blood-coagulation has been specially studied by Prof. Alex. Schmidt, and has been shown by this observer

to depend largely upon the white blood-corpuscles. The fibrin is formed by the union of two fibrin generators—fibrinogen and paraglobulin, and this union is effected by a fibrin ferment. The fibrinogen exists as such in the liquor sanguinis, but the ferment and the greater part of the paraglobulin are contained in the white blood-corpuscles. A destruction of some of these corpuscles and the liberation of the ferment and paraglobulin is therefore necessary in order for coagulation to take place.

The fluidity of the blood during life is due to its continuous contact with the living walls of the heart and bloodvessels. Whatever, therefore, interferes with this continuous contact, or impairs the vitality of the vessels in which the blood circulates will, by leading to the destruction of some of the white corpuscles, prevent fluidity and cause coagulation. An interference with the continuous contact of the blood with the vascular walls results from retardation of the blood-flow. Impairment of vitality of the vessels must involve the endothelium in order for it to cause coagulation—as long as the endothelium remains normal alterations in the walls of the vessels will not cause thrombosis. In many cases the coagulation is due partly to retarded blood-flow and partly to abnormal endothelium.

1. *Thrombosis from Retardation of the Blood-flow* may result from—

a. *Interruption or narrowing of the vessel.*—This occurs after the application of a ligature. Coagulation commences at the point of contact, and extends as far as the first large collateral branches, thus permanently closing the vessel. The laceration of the inner coat of the artery by the ligature, and the folds into which it is thrown, contributes very materially to the formation of the clot. The pressure exercised by tumors, cicatricial tissue, extravasations of blood, and the closure of a vessel by the impaction of an embolus, may in the same way by impeding or arresting the circulation cause thrombosis. General obstruction in the capillaries of a part also causes coagulation in the adjacent veins.

β. *Solution of the continuity of the vessel.*—The formation of a thrombus after the division or tearing of a vessel constitutes the means by which hemorrhage is immediately arrested—there must be either thrombosis or continuous hemorrhage. In the arteries, the severed end of the vessel contracts and retracts within its sheath, coagulation commences around it and extends upwards as far as the first large collateral branch. In the veins, hemorrhage is frequently

arrested by the valves, and the formation of a thrombus will evidently depend upon the relative situations of the valves and collateral vessels. The hemorrhage from the uterus after the separation of the placenta is arrested either by uterine contraction or by thrombosis. In all these cases the injury to the walls of the vessels is an important element in the causation of the coagulation.

γ. Dilatation of the vessel, or of the heart.—The most familiar example of thrombosis from this cause is that which occurs in an aneurism. The greater the amount of dilatation the greater is the retardation of the blood-flow. The coagulation commences at the sides of the vessel, and may extend until it completely fills the cavity. It is often favored by atheromatous or other changes in the walls of the sac. Coagulation from the same cause is not uncommon in the dilated plexuses of the prostate gland. In the heart, thrombosis is most frequent in the auricles. It usually commences in the auricular appendix, where there is very little propulsive power, and it may gradually extend into the auricular cavity. It is also met with in the ventricles, commonly commencing here between the columnæ carneæ.

δ. Diminished cardiac power.—This is a common cause of thrombosis in the veins. The coagulation commences just behind the flaps of the valves, from which it gradually extends into the cavity of the vessel. This appears to be owing to the force of the current not being sufficiently strong to completely open the valves, and the blood consequently stagnates and coagulates behind them. The crural and iliac veins, the venous plexuses of the back, and the cerebral sinuses, are the situations in which thrombosis from this cause is most frequently met with. It occurs in the course of many chronic exhausting diseases in which the cardiac power becomes diminished, and is especially frequent in phthisis, cancer, etc. The state of the blood, which often has an abnormal tendency to coagulate, together with the quiescent condition of the patient, materially aids in causing the coagulation.

2. Thrombosis from Abnormal Conditions of the Vessels or of the Blood.

a. Causes in the vessels.—All those alterations in the walls of the vessels which are accompanied by loss or by marked impairment of the vitality of the endothelium cause thrombosis. The abnormal surface acts as a foreign body and the blood coagulates upon it, and it may continue to do so until the cavity of the vessel becomes filled with coagulum. Thrombi produced in this way are consequently stratified. The walls of a vessel may become altered as the result of

inflammatory processes, and inflammation was formerly regarded as the main, if not the only, cause of thrombosis; hence thrombosis in veins is frequently termed "phlebitis" even at the present day. Inflammation of veins is certainly rare as a *primary* condition, although it not unfrequently results from the formation of a thrombus; and when occurring primarily, inflammatory processes, both in the arteries and the veins, have their seat in the external and middle coats or in the deeper layers of the intima. They never commence in the lining membrane of the vessel; this only becomes affected secondarily. The endothelium may be thrown off or die as the result of the inflammatory process, and when this has occurred the blood coagulates. Such inflammatory changes occur in the arteries, constituting the condition known as "atheroma," which, in the smaller vessels, may be a cause of thrombosis. In the heart they constitute endocarditis; and here also coagulation may take place upon the abnormal surface of the inflammatory vegetations. (See "Endocarditis.")

The walls of a vessel may also become altered, and thus thrombosis result, from inflammation or necrosis of the tissues in which it is situated. The vitality of the vessel becomes destroyed and the blood coagulates within it; and by this means the occurrence of hemorrhage is frequently prevented. Traumatic injury as a cause of thrombosis is exemplified by ligature, and by laceration or division of the vessel. In certain infectious diseases the endothelium undergoes fatty degeneration, and hence there is a tendency to coagulation¹. Lastly, the projection of new formations, as sarcoma, into the cavity of vessels causes the formation of a thrombus.

β. *Causes in the blood.*—There can be no doubt that certain conditions of the blood favor coagulation, and consequently tend to promote the occurrence of thrombosis. The phenomenon of blood-coagulation, as already stated, depends upon the white blood-corpuscles, and it is well known that, under certain circumstances, an increase in the number of these corpuscles in the blood favors the formation of thrombi. Such an increase is frequently met with in inflammatory processes which involve largely the lymphatic organs (leucocytosis). It is probable that other conditions of the blood, such as a loss of its serum, and alterations produced by fevers and by septic poisons, may also favor coagulation. (See "Septicæmia.") An increased tendency

¹ Pontiek. *Virchow's Archiv.* lx. p. 153.

of the blood to coagulate has long been known to exist in many acute inflammatory diseases, and in the latter months of pregnancy.

An increased tendency of the blood to coagulate, to whatever circumstances it may be due, is, however, probably never sufficient in itself to determine the formation of a thrombus; it can hence only be regarded as a predisposing cause. It is especially in those conditions, in which the circulation is impeded from diminished cardiac power, that it becomes an important agent in producing thrombosis.

CHARACTERS, ETC., OF THROMBI.—The thrombus may completely or partially fill the cavity of the vessel. In most cases, however, when coagulation has commenced, it proceeds until the vessel is obstructed, and when once this has occurred, the formation of the thrombus continues to extend in the course of the vessel until it meets with a current of blood strong enough to arrest its progress. Its ultimate extent will thus mainly depend upon the vessel in which it is formed, upon the size and situation of the collateral branches, and upon the force of the circulating current. The direction in which the coagulation principally extends, whether in the arteries or the veins, is consequently backwards, from vessels of smaller to those of larger calibre; the formation of the thrombus continuing until it meets with a current sufficiently strong to restore the circulation, which in many cases is as far as the entrance of the next large collateral vessel. For the same reasons the extension of thrombi is usually much greater in veins than arteries. In the capillaries, coagulation occurs only as the result of necrosis of the capillary walls, consequently in thrombosis from retardation of the circulation the coagulation will not extend in these vessels. The end of the thrombus next the heart is rounded and conical in shape. (See Fig. 68, c.)

Thrombi must be distinguished from the coagula that form after death, and also from those formed in the last moments of life which are so commonly found in the cardiac cavities. Post-mortem coagula are soft, and are often divisible into two layers, colored and uncolored; they do not adhere to the walls of the vessel, and rarely completely fill its cavity. The clots formed in the heart just before death constitute a connecting link between post-mortem coagula and thrombi. They are more or less decolorized, and are firmer in consistence and more fibrinous than post-mortem clots. They are not firmly adherent to the cardiac walls, but are often so entangled amongst the columnæ carneæ, chordæ tendineæ, and papillary muscles, that they cannot be quite readily separated. They appear to be the result of the mechani-

cal defibrination of the blood by the cardiac contractions a little while before death; the contractions not being sufficiently strong to empty the cavities, some of the blood remains behind, and becomes "whipped up" and defibrinated. These clots are most common in the right cardiac cavities, and they often extend some way into the pulmonary artery, from which, however, they can be very readily removed. They are met with most frequently in those cases in which the death-struggle has been prolonged, and in which there has been a gradual loss of power in the cardiac contractions. The existence of any increased tendency of the blood to coagulate will also materially favor their formation.

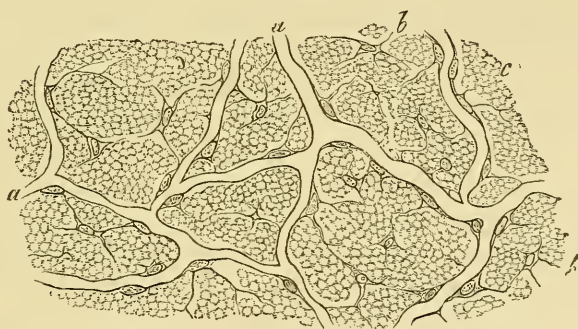
A *thrombus*, or ante-mortem clot, is firmer, dryer, and more fibrinous than either of the preceding, and it is *adherent* to the walls of the vessel. Its characters, however, vary with its age, and according as it originates in quiescent or circulating blood. When coagulation takes place in quiescent blood, as, for example, in an artery or vein after the application of a ligature, the thrombus when freshly formed is of a dark red-color and soft gelatinous consistence, closely resembling a post-mortem clot. It gradually loses its serum and so becomes dryer, less elastic, and more friable; but as the red corpuscles are contained in it, it still keeps its red color. The coagulation also taking place throughout the whole mass of blood, the thrombus maintains a more or less *uniform* structure. When, on the other hand, as is much more frequently the case, coagulation occurs in a vessel in which the blood is still circulating, as for example in the sac of an aneurism or on an inflamed cardiac valve, the thrombus presents quite different characters from the foregoing. Here the first step in the formation of the thrombus is the continuous adhesion of white blood-corpuscles to the abnormal surface of the vessel; then upon the little mass of adherent corpuscles fibrin is deposited, more corpuscles adhere, more fibrin is again deposited, and thus a more or less *stratified* thrombus is produced. In most cases but few of the red corpuscles get entangled in this process, so that these thrombi are never so red as the other variety, but are usually of a grayish-white color. The red blood-corpuscles contained in thrombi gradually atrophy and disappear, and their coloring matter is partly absorbed and partly converted into pigment. The thrombus thus becomes *decolorized*.

The subsequent changes which thrombi undergo are *organization* and *softening*.

Organization.—This is most frequent in the uniform unstratified thrombi, and especially in those occurring in arteries. The process consists in the gradual transformation of the thrombus into vascularized connective tissue. A thrombus which is undergoing a process of organization gradually diminishes in size, it becomes more and more decolorized, firmer and more fibrous in consistence, its union with the wall of the vessel becomes more intimate, and ultimately it may become converted into a fibro-cellular cord. These changes, although still imperfectly understood, probably originate in the wall of the thrombosed vessel and not in the thrombus itself.

Soon after the formation of the thrombus the red corpuscles, as already stated, disappear, but young cells resembling leucocytes are found in considerable numbers. Numerous new bloodvessels then make their appearance, intersecting the thrombus in all directions, and also some spindle-shaped and anastomosing cells. (Fig. 66.)

FIG. 66.

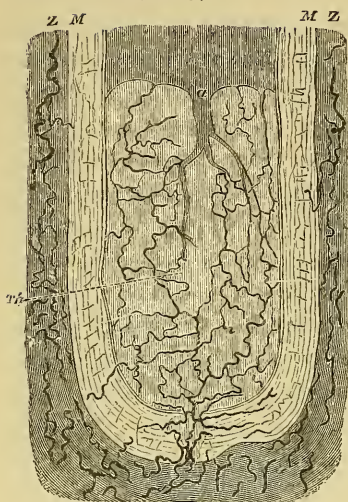


Section of an Arterial Thrombus Thirty-seven Days Old.—*a.* New bloodvessels.
b. Leucocytes and anastomosing cells. (Rindfleisch.)

These new cells communicate with the cavity of the thrombosed vessel, and with its vasa vasorum. (Fig. 67.) The thrombus thus becomes replaced by a vascular fibrillated structure which gradually undergoes a process of atrophy and contraction, and the new vessels disappear. In the process of contraction sinuses are often formed, by means of which the circulation is partly re-established. In some cases the thrombus becomes calcified, and thus forms a phlebolith.

The new vessels which penetrate the thrombus undoubtedly originate mainly from the vasa vasorum. Respecting the source from which the new cells which make their appearance are derived—it

FIG. 67.



Longitudinal Section of the Ligatured End of the Crural Artery of a Dog, Fifty Days after the Application of the Ligature.—Showing the newly-formed vessels in the thrombus and their communication with the vasa vasorum. *Th.* Thrombus. *M.* Muscular coat. *Z.* External coat and vasa vasorum. $\times 20$. (O. Weber.)

appears to be probable that they originate partly from the white blood-corpuscles, and partly from the endothelial and connective tissue cells belonging to the walls of the vessel. Recent researches tend to show that the endothelium takes a prominent part in the process. Whether, however, they are all of them the offspring of these elements, or whether some of them may not be leucocytes which have penetrated from without, is unknown. From these small cells the elongated connective-tissue cells are produced. The exact source from which fibrillated intercellular material is derived—whether the intercellular coagulum itself fibrillates, or whether it disappears and the fibres are derived from the protoplasm of the cells—is uncertain.

Softening.—If the thrombus does not become organized it usually undergoes a process of softening. This is most common in stratified thrombi, and especially in those occurring in the veins and heart. It is probable that in some cases the thrombus may become partially or completely absorbed. The softening usually commences in the centre of the clot, and gradually extends towards the circumference. In one form of softening the thrombus becomes converted into a reddish-brown, soft, pulpy material, which sometimes has the appearance of pounded cooked meat. Under the microscope it is seen to consist of albuminous granules, molecular fat, and more or less altered red and white blood-corpuscles. The whole of the thrombus may become softened, or the process may be limited to the more central portions, whilst the external layers become organized. Very frequently, as the older portions of the clot are becoming disintegrated and softened, fresh coagulation takes place at its extremities. The thrombus may also become perforated by openings through which the circulation is re-established. This, which may occur in softened as in organized thrombi, constitutes what is known as *canalization* of the thrombus.

Much more important than this simple red softening of thrombi is what has been described by Virchow as yellow or puriform softening. Here the central portions of the thrombus consist of a yellow or yellowish-red material which in consistence and appearance closely resembles pus. The walls of the vessel within which puriform softening of a thrombus is taking place almost invariably sooner or later become inflamed, and it was formerly believed that the puriform material was true pus and resulted from the inflammation of the vessel. (See "Results.") It is not however pus, but simply the softened and diffuent thrombus. It contains a few cells resembling pus-cells which are for the most part the leucocytes originally contained in the clot, and possibly also some may have entered from without. The puriform material is characterized physiologically by the property it possesses of inducing inflammatory and necrotic changes in the tissues with which it comes into contact. This property is due to the influence of *bacteria*; and to the presence and action of these organisms is probably also to be ascribed the puriform transformation of the thrombus. These septic changes in thrombi are intimately associated with the pathology of septicæmia and pyæmia, and they will be considered further when treating of these subjects.

RESULTS.—The results of thrombosis comprise certain changes in the walls of the vessels, more or less obstruction to the circulation, and embolism. These must be considered separately.

1. *Changes in the vessels.*—More or less alteration in the wall of the vessel is an invariable consequence of the formation of a thrombus. When the thrombus undergoes a process of organization, it becomes, as already described, intimately united with the vascular wall. The latter in the first place becomes infiltrated with cells and considerably thickened, but ultimately, together with the thrombus, gradually atrophies. It is when the thrombus is septic and undergoes a process of yellow or puriform softening that the most important changes take place in the vessel. These changes are of an acute inflammatory nature, and result from the injurious influence of the thrombus. They are most frequently observed in the veins, where septic thrombi are most liable to occur.

The walls of a vein within which a thrombus is undergoing a process of puriform softening are considerably thickened, so that the vessel more resembles an artery. The inner surface has lost its translucency, and is of a dead opaque color. The adventitia and middle coats are hyperæmic with numerous hemorrhagic points, which latter

are often visible through the intima. Somewhat later the walls of the vessel become infiltrated with leucocytes, small collections of pus are seen in the external and middle coats, and portions of the intima may become detached. The neighboring tissue may also become involved. These acute inflammatory changes in veins constitute what is known as *suppurative phlebitis*. Although they are most frequently due to thrombosis, they may also occur as the result of extension from adjacent suppurating tissues, in which case the thrombus, which also undergoes puriform softening, is *secondary* to the phlebitis. (See "Inflammation of Veins.") Similar changes are observed in the arteries.

2. *Obstruction to the circulation*.—The consequences of the obstruction to the circulation which results from the formation of a thrombus will depend upon the rapidity and cause of its formation, the nature and size of the vessel obstructed, the situation and number of the collateral branches, and the force of the circulating current. The rapidity with which the obstruction is effected is of considerable importance, inasmuch as the more gradual this is the longer is the time allowed for the establishment of a collateral circulation. For this reason the interference with the circulation caused by thrombosis is, for the most part, less marked than that which results from the more sudden obstruction caused by embolism. The cause of the thrombosis is important for the reason already stated—viz., that in that which results from retardation of the circulation the coagulation does not extend in the capillary vessels.

In the veins when thrombosis occurs in a vessel of small size and there are numerous collateral branches, as in the prostatic or uterine plexuses, the circulation is but little interfered with, and no symptoms of obstruction result. If, however, the main trunk of a large vein becomes obliterated, as that of the femoral or iliac veins, the obstruction is followed by hyperæmia, the extent and duration of which will depend upon the facility with which the circulation can be restored by the collateral vessels. Thrombosis in the above-named veins frequently occurs, as already stated, in the latter stages of many chronic debilitating diseases, especially in phthisis; also in the puerperal state, where it gives rise to the condition known as *phlegmasia dolens*. The formation of a thrombus here is followed by oedema and swelling of the limb, which becomes tense, elastic, and painful. In the early stage there may be some cyanosis, but this is usually quickly followed by a pallid whiteness of the surface. There is often more or less

tenderness in the course of the vein, which feels enlarged, hard, and knotted, owing to the secondary inflammatory changes in its walls. At the same time there is sometimes swelling and tenderness of the lymphatics, which may be seen as red lines traversing the limb. Diffuse inflammation of the skin and subcutaneous cellular tissue occasionally occurs. These changes are owing partly to the mechanical impediment to the circulation, and partly to the obstruction of lymphatics and to the secondary inflammatory processes in the vein and tissues which ensue. The circulation is usually ultimately restored; but if the impediment has been of long duration, the tissues become thickened, and the limb is left in a hard, indurated, and somewhat enlarged condition.

The results of obstruction in arteries have been already considered in the chapter on Local Anæmia. These results will obviously depend upon the facility with which the circulation can be restored by the collateral vessels. If the circulation be quickly re-established, the vitality of the tissues may not become impaired; but if not, the part may undergo a process of molecular disintegration and softening, the softened tissue often being surrounded by a zone of hyperæmia which results from the attempt to establish a collateral circulation. It is in tissues with terminal arteries that the interference is most marked, and here the hemorrhagic infarction which so often results from embolism may occur, although owing to the more gradual obstruction of the circulation, it is less likely to do so. (See "Embolism.")

3. *Embolism*.—Portions of the thrombus may be carried away by the circulation, thus constituting embolism. This, which is the most important result of thrombosis, will be considered in the following chapter.

CHAPTER XXVII.

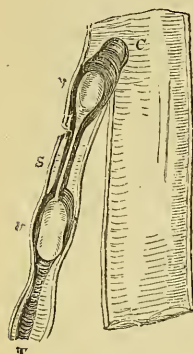
EMBOLISM.

EMBOLISM is the arrest of solid substances circulating in the blood in vessels which are too small to allow them to pass. The solid substances are termed *emboli*. These are very various in their nature.

By far the most frequent source of emboli are thrombi, portions of

which are carried from the seat of their formation by the circulation, and become arrested in distant vessels—thus constituting embolism. A thrombus may give rise to emboli in various ways. It may soften and break down, and if the lumen of the vessel be thus restored, its fragments become distributed by the blood-current. In those cases in which the thrombus does not fill the vessel, portions of it may readily be carried away by the blood passing over it. Perhaps, however, the most frequent way in which a thrombus gives rise to embolism is by its conical end being broken off by the current of blood from a collateral vessel. The formation of a thrombus, as already described, usually ceases opposite the entrance of a large

FIG. 68.



A Thrombus in the Saphenous Vein.—Showing the projection of the conical end of the thrombus into the femoral vessel. *S.* Saphenous vein. *T.* Thrombus. *C.* Conical end projecting into femoral vein. At *v*, opposite the valves, the thrombus is softened. (Virchow.)

collateral vessel, and if its conical end project a little way into the cavity of this vessel it may be readily broken off by the blood-current. (Fig. 68.) It is especially venous thrombi which give rise to embolism; the veins of the leg, the iliac, hypogastric, and jugular veins being amongst the most common sources. Emboli from cardiac thrombi are also exceedingly common, whilst those from arterial are the least frequent. In embolism originating from a thrombus, some sudden movement or exertion often determines the separation of the embolus.

Emboli may, however, originate independently of thrombi:—vegetations and calcareous or atheromatous masses separated from the valves of the heart, or from the inner surface of arteries; portions of new growths, as carcinoma, which having perforated the vessels, have been carried away by the current; parasites which have made their way into the interior of vessels; fluid fat which has escaped from the fat-cells and entered ruptured bloodvessels, such as occasionally occurs in fractures of bone, etc.; pigment granules, and other substances, may all constitute emboli.

The emboli become arrested in the first vessels they meet with which are too small to allow them to pass; the size of the vessel will consequently depend upon the size of the embolus. They are often so minute that they pass into and become impacted in the smallest capillaries. The seat of impaction is usually at the bifurcation of

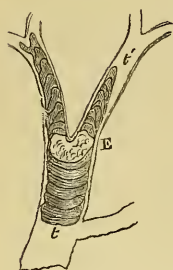
the vessel, or, where, from the giving off of branches, the calibre is diminishing rapidly. (See Fig. 69.) Thus emboli originating in the systemic veins or in the right cardiac cavities, will most commonly become arrested in the vessels of the lungs; those originating in the arteries, the left cardiac cavities, or the pulmonary veins—in the systemic arteries and capillaries, especially in those of the spleen, kidneys, and brain; and those originating in the portal venous system—in the hepatic branches of the portal vein. In some cases, however, the smallest emboli may pass through the capillaries of the lungs and become arrested in those of the kidneys, spleen, or other organs. Thus, with the exception of emboli originating in the portal vessels, the seat of arrest is the arteries or capillaries.

The emboli are usually carried in the direction of the main current; hence those carried by the aortic stream more commonly pass into the thoracic aorta than into the carotid and subclavian vessels, and into the left carotid and renal artery than into the corresponding arteries of the opposite side. Gravitation also influences the direction in which they are carried, especially those of large size, which move somewhat more slowly than the blood-stream. Owing to this they are more common in the lower lobes and posterior parts of the lungs than in the superior and anterior portions of these organs.

The embolus, when arrested, may either completely or only partially fill the cavity of the vessel. If, as is frequently the case, the arrest takes place at a point of bifurcation, the embolus may partially fill both branches, allowing a small stream of blood to pass. This may break off portions of it, and so cause secondary emboli, which become impacted in more distant vessels. The amount of obstruction which immediately follows the arrest will partly depend upon the nature of the embolus itself. If the embolus be from a soft, recently formed thrombus, it will adapt itself to the cavity of the vessel, and so completely occlude it. If, on the other hand, it is irregular in shape and firm in consistence, as when derived from a calcified cardiac vegetation, it may not fill the vessel, but allow a small current of blood to pass it.

The arrest of the embolus, and the consequent obstruction to the circulation, is followed by the formation of thrombi behind and in front of it, which extend as far as the entrance of the first large collateral vessels. (Fig. 69.) If the embolus does not completely fill the vessel, coagulum is deposited in successive layers upon its

FIG. 69.



Embolus impacted at the Bifurcation of a Branch of the Pulmonary Artery.— Showing the formation of thrombi behind and in front of it, and the extension of these as far as the entrance of the next collateral vessels. *E.* Embolus. *tt'*. Thrombi. (Virchow.)

surface until the occlusion of the vessel is complete, and then the secondary thrombus extends, as in the former case, until it meets with a current of blood strong enough to arrest its progress. If the embolus is a portion of a soft thrombus, it will in most cases be impossible to distinguish it from the secondary thrombus which surrounds it. If, however, it is a calcareous mass, or a portion of an old thrombus, it may usually be distinguished from the more recent secondary coagulum.

Emboli may, in rare cases, become absorbed. They may also, when derived from thrombi, become organized or softened. The changes in the secondary thrombi are similar to those already described as occurring in the primary—comprising adhesion to the wall of the vessel, softening, and organization.

RESULTS.—The results of embolism are of two kinds—those depending upon the mechanical obstruction to the circulation, and those produced by the irritating or infective properties of the emboli themselves.

Changes in the Obstructed Vessels.—The first series of changes are those occurring in the walls of the vessel within which the embolus becomes arrested. These changes depend upon the mechanical and physiological properties of the embolus. If the embolus possesses no infective properties, being derived from a source where no septic changes are taking place, it, together with the thrombus which it causes to form around and beyond it, usually becomes organized or reabsorbed, and the walls of the vessel become more or less thickened. Or, if the embolus has rough surfaces, as when derived from a calcareous vegetation in the heart, it may produce some inflammation of the vessel. When, on the other hand, the embolus is impregnated with septic pus, or with other putrid inflammatory products, it causes an inflammation and sloughing of the walls of the vessel within which it is impacted, which may extend for some distance into the surrounding tissues, precisely similar to what has been already described as occurring in the walls of a vein which contains a puriform thrombus.

The vessels also undergo important changes as the result of deprivation of arterial blood. Owing to these changes, which have been already described in the chapter on Local Anæmia, the vessels lose their power of retaining the blood, allowing the liquor sanguinis and

blood corpuscles to escape, and ultimately they become necrotic and rupture. (See "Hemorrhagic Infarction.")

Allusion must be made here to embolism as a cause of aneurism. That aneurisms, especially of the cerebral arteries in young people, are often due to embolism is now pretty generally admitted by pathologists. With regard to the mode in which the embolus causes dilatation of the artery, although this may differ in different cases, an injurious influence of the embolus upon the walls of the artery, and a consequent inflammatory softening of the vessel, is probably the most common condition.

Changes in the Organ.—Important changes take place in the organ or tissue, the vessels of which have become plugged by the embolus. The first effect of the plugging of a vessel by an embolus, is the arrest of the circulation through it, and if the vessel be the main nutrient or functional artery, this is followed by the sudden cessation of the function and nutrition of the part. Thus, plugging of one of the larger arteries in the brain is followed by sudden loss of consciousness and paralysis (apoplexy); plugging of the pulmonary artery, by sudden asphyxia; and of the coronary arteries, by sudden paralysis of the heart. The subsequent changes will depend upon the structure of the organ, the arrangement of its vessels, the facility with which a collateral circulation can be established, and the nature of the embolus. If the circulation be quickly restored by the collateral vessels, a sufficient arterial anastomosis being established behind the obstructed artery, the part recovers itself without undergoing any structural change, and its nutrition and functions are restored. If, however, this is not the case, the vessels and surrounding tissues may ultimately lose their vitality. The interference with the circulation is partly due to the thrombosis which occurs around the impacted embolus. The organs in which the arrangement of the blood-vessels is such that the circulation cannot be readily restored by the anastomosing vessels, and consequently those in which necrotic changes most commonly result from embolism, are the spleen, the kidneys, the lungs, the brain, and the retina. (Fig. 70.) These arteries with which anastomoses do not exist are called by Cohnheim, as already stated, "terminal" arteries. (See "Local Anæmia.") The area of tissue from which the supply of blood has been cut off is usually surrounded by a zone of intense hyperæmia, which results from the stress which is thrown upon the collateral vessels. The zone of hyperæmia is very characteristic, and indicates at once the nature of the lesion.

When, owing to the absence of sufficient arterial anastomosis (when terminal arteries are blocked), the circulation cannot be restored, the

FIG. 70.



Embolic Kidney.—From a case of aneurism of the abdominal aorta. Numerous small yellowish-white patches were seen scattered through the cortices of the organs. $\times 200$.

vessels in the embolic area become so much altered that exudation, emigration, and hemorrhage may take place, and thus may be produced a tract of tissue within which the circulation has become arrested, and which is more or less extensively infiltrated with blood.

This is known as a *hemorrhagic infarct*. These hemorrhagic infarcts are very frequently met with, especially in the lungs, spleen, and kidneys. They are blackish red, firm masses of consolidation, and owing to the distribution of the blood-vessels they are usually wedge-shaped, the apex of the cone being towards the centre of the organ. The more complete the obstruction and the more vascular the tissue, the greater is the amount of infarction, and the more rapid is the softening and disintegration that ensues. (Fig 71.)

FIG. 71.

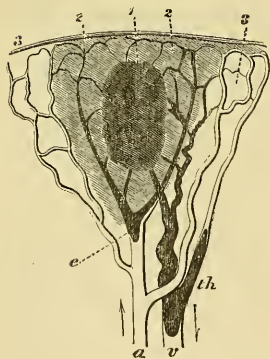


Diagram of a Hemorrhagic Infarct.—*a*. Artery obliterated by an embolus (*e*). *v*. Vein filled with a secondary thrombus (*th*). 1. Centre of infarct which is becoming disintegrated. 2. Area of extravasation. 3. Area of collateral hyperæmia. (O. Weber.)

This vascular engorgement of the embolic area was formerly supposed to be due to the increased stress which is thrown on the collateral vessels. The investigations of Cohnheim, however, already alluded to, show that it is really mainly owing to the

fact that when the force of the blood stream in the artery is annihilated by the impaction of the embolus, there is a backward pressure and regurgitation from the veins into the capillaries, so that there is produced considerable venous engorgement of the last-named vessels. The vitality of the vessels gradually becoming so much impaired that they are unable to retain the blood, this escapes into the tissues. (See "Local Anæmia.") The infarction consequently does not occur immediately after the impaction of the embolus, but only after the lapse of a certain time.

The subsequent changes which take place in the infarct depend upon its size, upon the extent to which the circulation in it is interfered with, and upon the nature of the embolus which caused the infarction. If the infarct is small and the embolus possesses no septic properties, the coagulated blood may gradually become decolorized, and the mass undergo a gradual process of absorption. The infarct then changes from a dark red to a brown or yellow tint, its more external portions become organized into connective tissue, and the whole gradually contracts, until ultimately a cicatrix may be all that remains to indicate the change. If, however, the infarction is considerable, the central portions may undergo a certain amount of molecular disintegration and softening. This may subsequently dry up and become encapsuled. In all these secondary changes which take place in the infarct, its most external portions are surrounded by a red zone of hyperæmic tissue. This is exceedingly characteristic.

If an embolus possesses septic properties, as when it is derived from a part where putrefactive inflammatory changes are going on, it sets up similar inflammatory processes both in the vessel within which it becomes impacted, and also in the surrounding tissues. These septic inflammatory changes lead to the formation of abscesses, which are known as *embolic* or *metastatic abscesses*. The formation of the abscess may be associated with more or less infarction and necrosis of the embolic area. Colonies of bacteria are almost invariably found in these abscesses, and it is to the presence of these organisms that the infective properties of the embolus are probably due. This subject will be considered further in the chapter on "Septicæmia and Pyæmia."

Thrombosis and Embolism of the Brain.

Thrombosis and embolism are the most common causes of *cerebral softenings*.

Softening from Thrombosis.—This is commonly the result of atheromatous, calcareous, or syphilitic changes in the cerebral arteries. Such changes cause a diminution in the lumen or a roughening of the internal surface of the vessels, impair their elasticity and contractility, and so favor the occurrence of thrombosis. As a result of the interference with the supply of blood, the cerebral substance undergoes a more or less rapid process of necrosis, such as has been already described. (See “Cerebral Softening.”) The softened portions, when recent, and when the obstruction is rapidly induced, are often of a reddish color, although with age they gradually become decolorized. In the more gradually induced obstructions the color of the softened tissue is usually white.

Softening from Embolism.—The softening resulting from embolism is, for the most part, entirely dependent upon the obstruction to the circulation caused by the embolus and by the resulting thrombosis. It is rapidly induced and is often attended by the extravasation of blood, when it constitutes one form of acute red softening. If the interference with the circulation be slight, there may be no extravasation of blood and the process of disintegration may be more gradual, so that the softened portions are white in color, and the condition then more resembles the chronic white softening already described as resulting from degeneration of the cerebral bloodvessels. (See “Cerebral Softening.”) The softened tissue will also be white in color when one of the large vessels is obstructed, so that a large portion of one hemisphere loses its vitality. The vessel most frequently blocked is the middle cerebral artery, in some part of its course; and in the majority of cases it is that of the left side. In almost all cases in which softening of the cerebral substance results from embolism, the embolus is arrested in one of the vessels beyond the circle of Willis, because here the circulation cannot be readily restored by the collateral vessels.

When the interference with the circulation is attended by vascular engorgement and extravasation of blood, the softened portion, in the early stage, is either of a uniform dark-red color, or presents numerous red hemorrhagic points. The softening is most marked in the centre, whilst the hyperæmia and redness may extend for some dis-

tance around it. Under the microscope, the softened portion is seen to consist of broken-down nerve fibres, altered blood-corpuscles, granules of fat, and the large granular corpuscles already described. (See Fig. 15.) The surrounding capillaries are dilated and filled with coagula, and the granular corpuscles envelop their walls. In a more advanced stage all trace of nervous structure is lost, the softened mass becomes decolorized, and passes from a dark-red color to a chocolate, brown, yellow, or even white. It may liquefy and form a cyst; more commonly, however, it gradually dries up, and a process of repair takes place by the growth of the surrounding neuroglia, which forms a fibrous network in the place of the softened tissue. This contracts, and ultimately a cicatrix with hæmatoidin crystals may be all that remains.

Red softening from embolism is often very difficult to distinguish in the post-mortem room from that which results from thrombosis.

CHAPTER XXVIII.

LEUKÆMIA.

LEUKÆMIA, or leucocythæmia, is a disease characterized by a considerable and permanent increase in the number of white corpuscles of the blood, by a diminution in the number of the red corpuscles, and by enlargement of some of the lymphatic organs. The lymphatic organ most frequently involved is the spleen. This is enlarged in the great majority of cases (Splenic Lukæmia). The enlargement of the spleen is sometimes associated with enlargement of the lymphatic glands, and sometimes, although much less frequently, with an increase in the medulla of bones. In rare cases the lymphatic glands only are involved (Lymphatic Lukæmia), and cases have been described by Neumann and others in which the osseous medulla was principally affected. In most cases of leukæmia an overgrowth of lymphatic tissue in other organs occurs sooner or later in the course of the disease.

Leucocytosis.—Before proceeding with the consideration of leukæmia it will be well to allude briefly to that slight and temporary increase in the number of white blood-corpuscles which has been termed “leucocytosis.” This differs essentially from leukæmia in

this respect, that the increase in the number of white corpuscles is only temporary, and is not necessarily associated with any diminution in the number of the red. Further—the increase is never nearly so great as in leukæmia, rarely more than forty or fifty being seen in the quarter-inch field of the microscope.

Such slight and temporary increase in the number of white blood-corpuscles occurs in many conditions. Physiologically, it occurs after a meal, and in the latter months of pregnancy. In many of the acute pyrexial diseases, especially in those in which there is acute swelling of lymphatic structures, as in typhoid and scarlet-fever, and in septicæmia, there is often a marked excess of white corpuscles. After large losses of blood also, there is an increase. These conditions are only temporary, and do not appear to interfere either with the circulation or with the general health.

PATHOLOGY.—The pathology of leukæmia is still exceedingly obscure, and will probably remain so until our knowledge of the physiology of the blood and the origin and fate of the blood-corpuscles is more complete. Physiologically, we know that the white corpuscles originate in the lymphatic organs, from which they pass into the blood, either directly or through the lymphatic vessels; and it is now generally believed that the red corpuscles originate from the white, the latter being transformed mainly in the spleen. Owing to the enlargement of one or more of the lymphatic organs which always exists in leukæmia, it has been supposed that the increase in the number of the white corpuscles which characterizes the disease is due to their excessive production by the enlarged organs, such as occurs in some cases of leucocytosis. Inasmuch, however, as there is not only an increase in the number of white, but a diminution in the number of red, this hypothesis is insufficient to account for the blood change. Further—lymphatic organs may become enormously

enlarged without the production of any leukæmia. This occurs, for example, notably in the spleen in *Splenic Anæmia*, which disease, with the exception of the increase in white blood-corpuscles, is precisely similar to leukæmia; and also in the lymphatic glands in Hodgkin's disease. Although, as already stated, the subject is still involved in much obscurity, the view promulgated by Virchow more than twenty years ago accounts most

FIG. 72.



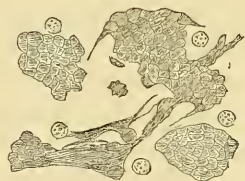
Leukæmic Blood.—From a young man aged twenty-four, with enormous enlargement of the spleen. $\times 200$.

satisfactorily for the blood change:—it is that the normal transformation of white corpuscles into red is imperfectly performed, so that not only is the number of white increased, but that of the red diminished. It is probable that this diminished transformation of the white corpuscles is the most important element in most cases of leukæmia, although it may be associated with an increased production. Both the diminished transformation and the increased production take place in the enlarged lymphatic organs, and all we can say at present in explanation of the process is, that the function of one or more of these organs is imperfectly performed. The enlargement of the lymphatic organs is with little doubt due to new growth, and not, as has been suggested by some, simply to the accumulation within them of the white corpuscles which exist in such large numbers in the blood.

HISTOLOGY.—Blood.—The diminution in the number of white corpuscles varies very considerably in different cases. A proportion of one white to ten red is quite common, and often there are as many as one to three. (Fig. 72.) This increase gives to the blood a paler and more opaque appearance than natural. In the earlier stages of the disease the proportion may not be more than one to twenty or forty. The white corpuscles sometimes resemble the natural ones, but often they are somewhat larger and more granular. This is especially the case in splenic leukæmia, whereas when the lymphatic glands are principally affected, many of the corpuscles are usually smaller than natural. Some of them are often more or less fattily degenerated.

The red corpuscles, like the white, vary in the diminution of their number. They may be reduced to one half or a quarter the normal. They are usually natural in appearance, but sometimes they are distinctly paler than in health. Occasionally they appear to be unusually soft, and exhibit a tendency to stick together instead of forming the natural rouleaux. In a case of splenic anæmia recently under my care these characters were especially marked. (Fig. 73.) The diminution in the number and the impairment of the quality of the red corpuscles, which exists not only in leukæmia but in most cases of great splenic enlargement, accounts for the anæmia which exists in these conditions. In addition to the red and white corpuscles, Klebs and others have found nucleated red corpuscles in leukæmic blood; and minute, color-

FIG. 73.



Blood from a case of Splenic Anæmia.—From a middle-aged man with great enlargement of the spleen. $\times 200$.

less, octohedral crystals of an albuminous character have been discovered by Charcot and Zenker in the blood and certain organs. The coagulating power of the blood in leukæmia is much diminished, and when the liquid is allowed to stand the white corpuscles form a creamy layer upon its surface.

Spleen.—In this, which is much the most important organ in the production of leukæmia, the change is characterized mainly by increased growth. The organ becomes enlarged, and usually enormously so. The enlargement is uniform, so that the shape of the organ is but little altered. The capsule is often thickened, and there are usually adhesions with the adjacent viscera. The consistence in the later stages is commonly distinctly firmer than natural. The cut surface is smooth, of a grayish or brownish-red color, and thickened trabeculæ can often be seen marking it as whitish lines. The Malpighian corpuscles, although they may be slightly enlarged in the earlier stages of the disease, are seldom prominent, and they are often not visible when the splenic enlargement is advanced. In exceptional cases, however, and especially when the lymphatic glands are involved they may form prominent growths. Sometimes wedge-shaped masses of a dark red or reddish-yellow color are seen near the surface of the organ. These are probably infarctions of embolic origin.

When the spleen is examined microscopically, its structure is found to be but little altered, the enlargement being due mainly to an increase of the splenic pulp. The trabecular tissue is also increased and thickened, and becomes increasingly so as the splenic enlargement advances. The Malpighian corpuscles are but little increased in size, and sometimes they are atrophied.

Lymphatic Glands.—The enlargement of the lymphatic glands is much less in splenic leukæmia than in those cases in which the glands are primarily and principally affected. In splenic leukæmia one or more groups of glands are slightly enlarged in about one-third of the cases. The glands are rarely increased in consistence, and are usually freely movable. On section they are of a grayish-red color, often mottled with hemorrhages. Microscopically, the enlarged glands present a normal structure.

In some cases this excessive development of lymphatic structures takes place in other parts. The *follicles of the intestine*, and the *medulla of bone*, are those most commonly involved. In the intestines, the follicles may become so much enlarged as to form distinct projections from the mucous membrane, although this is less common

than in Hogkin's disease. The enlarged follicles may also ulcerate. The medulla of bones is occasionally increased, and, as already stated, cases have been described in which this tissue was primarily and principally affected. It is increased in quantity and altered in quality. It is usually softer than natural, and of a grayish or grayish-yellow color. Microscopically, the fat cells are seen to be replaced to a great extent by lymphoid elements.

In the course of the disease a new growth of lymphatic tissue or an infiltration with lymphatic elements usually takes place in non-lymphatic structures, principally in the liver and kidneys, less frequently in the lungs and muscle. The new growth in these organs sometimes forms distinct tumors, but much more commonly exists as an infiltration. How far these lymphoid growths are the result of a hyperplasia of the cells in the interstitial tissue of the organ in which they are situated, and how far an emigration of the leucocytes, which exist in such large numbers in the blood, takes part in their formation, is unknown. The former, however, is probably the most important factor in the process.

The organ which is most frequently affected is the *liver*. Here the vessels generally are enlarged and distended with white blood-corpuscles. Accumulations of corpuscles and lymphoid tissue are seen between the acini, and extending along the intercellular network into the acini themselves, so that the lobules are sometimes seen to be clearly mapped out by a grayish-white interlobular infiltration. As this increases, the liver-cells become compressed and atrophy, until ultimately the lobules may be replaced entirely by it. Associated with this infiltration there is usually a formation of small, round, whitish lymphoid nodules, somewhat resembling gray tubercles. These also are situated in the interlobular tissue. Owing to these changes, the liver becomes very considerably increased in size.

In the *kidneys*, which are also frequently affected, the change is similar to that in the liver. Here also it consists for the most part in an infiltration, with which may be associated the formation of roundish nodules and masses.

CHAPTER XXIX.

INFLAMMATION.

THE morbid processes which have thus far been described have been characterized mainly by alterations in the nutritive activity of the histological elements of the tissues; or by changes in the circulation, or in the blood. In *inflammation* some alteration in the walls of the bloodvessels appears to be the essential part of the process.

Inflammation may be defined to be the succession of changes which takes place in a living tissue as the result of some kind of injury, provided that this injury be insufficient immediately to destroy its vitality. With regard to the nature of the injury—it may consist in some direct damage to the tissue, either by mechanical or chemical agents, or by substances conveyed to it by means of the bloodvessels or lymphatics; or the injury may be indirect, as in some cases of inflammation of internal organs arising from exposure to cold. In all cases, however, some injury of the tissue—an injury which impairs, and if not of sufficient intensity would destroy, its vitality—precedes the occurrence of the local changes which constitute the inflammatory process.

The exact nature of these changes has, for the most part, been ascertained during the past twelve years, mainly owing to the experimental researches of Professors Cohnheim, Stricker, and Burdon Sanderson. The method of investigation has consisted in the artificial production of inflammation in the lower animals, and the observation of the process as thus induced. The process comprises—

1st. *Changes in the bloodvessels and circulation.*

2d. *Exudation of liquor sanguinis and migration of blood-corpuscles; and*

3d. *Alterations in the nutrition of the inflamed tissue.—*

It will be well, in the first place, to consider each of these separately, in the order in which they occur, and subsequently to endeavor to point out how far a causal relation exists between them.

I. CHANGES IN THE BLOODVESSELS AND CIRCULATION.—Changes in the bloodvessels and circulation, resulting in increased vascularity,

have ever been regarded as playing a most important part in inflammation, as upon them principally depend those signs of the process which are most obvious during life. The redness, heat, and swelling, which are so constantly met with in inflamed tissues, are in great measure due to the attendant hyperæmia. The swelling, however, is in most cases dependent rather upon the effusion than upon the over-fulness of the bloodvessels.

These changes in the bloodvessels and circulation are essential constituents of inflammation, both in vascular and in non-vascular tissues. In the latter, which comprise the cornea and cartilage, they take place in the adjacent vessels from which these tissues derive their nutritive supply. The nature of these vascular changes has been studied by the artificial production of inflammation in transparent tissues, in which the circulation can be readily observed; the web, mesentery, and tongue of the frog, and the wing of the bat, being most convenient for this purpose. The phenomena, as observed in the mesentery of the frog, which has been previously curarized, may be thus briefly described:—

The first effect of injury of the mesentery—mere exposure to the air being sufficient for the purpose—is to cause *dilatation* of the arteries, and after some interval a similar dilatation of the veins and capillaries. The dilatation of the arteries commences at once, and is not preceded by any contraction. It gradually increases for about twelve hours, and is accompanied also by an increase in the length of the vessels, so that they become more or less tortuous. This enlargement of the bloodvessels is associated at the commencement of the process with an *acceleration* in the flow of blood; this, however, rarely lasts more than an hour, and is followed by a considerable *retardation* in the circulation, the vessels still remaining dilated. These alterations in the rapidity of the blood-flow cannot be owing to the increase in the calibre of the vessels, which remain throughout dilated.

It has, however, long been known that the acceleration of the blood-flow in an injured part—the so-called *determination* of blood, which was so correctly described more than thirty years ago by Dr. C. J. B. Williams, is not necessarily followed by retardation. It may gradually subside without retardation or any of the essential phenomena of inflammation taking place. Cohnheim has consequently stated in his more recent researches on inflammation, that the dilatation of the vessels and the increased velocity of the blood-current which ensue

immediately after the infliction of the injury are only temporary and accidental. They may even, in some cases, be followed by contraction before the permanent dilatation commences. The permanent dilatation and diminished velocity, on the other hand, come on slowly and are permanent, and these must be regarded as the proper vascular phenomena of inflammation. These proper phenomena may be induced without the previous occurrence of the accidental ones.¹

Returning to the observation of the frog's mesentery—the retardation of the circulation in the dilated vessels is sometimes seen to take place somewhat suddenly, and it is usually first observable on the venous side of the capillary network. As the blood-stream becomes slower, the *white* corpuscles, which naturally tend to move slowly along the sides of the veins, gradually accumulate in these vessels, and ultimately they may nearly fill them. The red corpuscles also accumulate, but more especially in the capillaries; and thus the veins and capillaries become filled with corpuscles. The circulation becomes slower and slower until in many of the vessels the blood almost completely stagnates, and the accumulated corpuscles oscillate slightly to and fro with the cardiac systole. This stagnation of the circulation in the dilated vessels constitutes the condition known as *inflammatory stasis*. Whilst these changes are taking place, the mesentery gradually becomes increasingly obscured by small cell forms. These are white corpuscles which have emigrated from the vessels. The phenomena of emigration will be considered subsequently.

II. EXUDATION OF LIQUOR SANGUINIS AND MIGRATION OF BLOOD-CORPUSCLES.—Another constituent of the inflammatory process consists in the exudation of the liquor sanguinis and the migration of the blood-corpuscles.

a. Migration of Blood-Corpuscles.—The migration of the white blood-corpuscles (leucocytes) through the walls of the bloodvessels was first described, although very incompletely, by Dr. W. Addison in 1842.² This observer stated as the result of his researches, that in inflammation these corpuscles adhered to the walls of the vessels and passed through them into the surrounding tissues. In 1846 Dr. Augustus Waller described more fully the same phenomenon, and from his description there can be little doubt that he actually observed

¹ "Neue Untersuchungen über die Entzündung," Cohnheim, 1873.

² "Experimental and Practical Researches on Inflammation." *Trans. Prov. Med. Association*, 1842.

the emigration of corpuscles.¹ Both these observers concluded that the escaped blood-corpuscles became pus-corpuscles. Their observations, however, were but little thought of and were soon forgotten, and it was not until 1867, when similar investigations were instituted quite independently by Professor Cohnheim, in Berlin—to whose minute researches we must ascribe most of our present knowledge on this subject—that the emigration of blood-corpuscles came to occupy an important place in the pathology of inflammation.²

The emigration may be observed in the mesentery of a frog which has previously been paralyzed by the subcutaneous injection of curare. The changes in the bloodvessels and in the circulation, and the accumulation of blood-corpuscles in the part, have been already described; it remains only to consider the phenomena of emigration.

The white blood-corpuscles (leucocytes) which have accumulated in large numbers, especially in the veins, remain almost stationary against the walls of the vessel, the blood-current and red corpuscles passing by them, although with much diminished velocity. Those immediately adjacent to the wall gradually sink into it, and pass through it into the surrounding tissue. In doing so they may be observed in the various stages of their passage. At first small button-shaped elevations are seen springing from the outer wall of the vessel. These gradually increase until they assume the form of pear-shaped bodies, which still adhere by their small ends to the vascular wall. Ultimately the small pedicle of protoplasm by which they are attached gives way and the passage is complete, the corpuscles remaining free outside the vessel. A similar emigration takes place, but to a less extent, from the capillaries. From the last-named vessels, however, the red corpuscles also escape although in fewer numbers; whilst from the arteries no emigration occurs. The escaped corpuscles are continuously replaced by fresh ones, and as the process proceeds the vessels become obscured by the leucocytes which surround them. In those portions of the inflamed tissue where absolute stasis has occurred no emigration takes place.

These phenomena can perhaps be better studied in a more localized inflammatory process, such as may be produced by the application of some injurious agent—a small piece of nitrate of silver, for example—to the tongue of the frog. Here, to quote from Cohnheim, in the

¹ *Phil. Magazine*, vol. xxix. 1846.

² "Ueber Entzündung und Eiterung:" *Virchow's "Archiv,"* vol. xl.

most central portion of the inflamed area—that which is the most injured, there is absolute stasis, the blood usually coagulates, and no emigration takes place. This is due to the vitality of the vessels being completely destroyed by the injurious agent. (See “Thrombosis.”) Outside this there is an area in which the blood is circulating very slowly, the capillaries are filled with red corpuscles, many of which escape; whilst more externally still, is an area in which the blood is less stagnant, and abundant emigration is taking place, the white corpuscles escaping from the veins and capillaries, the red from the capillaries alone. The central area, which usually dies, is thus surrounded by an enormous number of red and white corpuscles; and the red corpuscles which have accumulated in this area are so closely packed that their outlines can scarcely be distinguished.

β. *Exudation of Liquor Sanguinis*.—Associated with the passage of the blood-corpuscles through the walls of the vessels, is an exudation of the liquor sanguinis. The exuded liquor sanguinis—which constitutes the well-known *inflammatory effusion*—differs from the liquid which transudes as the result of increased pressure in the capillaries in mechanical congestion. (See “Mechanical Hyperæmia.”) It contains a larger proportion of albumen, more phosphates and carbonates, and has a much greater tendency to coagulate. This latter property is mainly due to the white blood-corpuscles which it contains. (See “Thrombosis.”)

The most characteristic feature of inflammatory effusion is the large number of cell-structures which it contains. The great majority of these are the white corpuscles which have escaped from the vessels. A much smaller number are the escaped red corpuscles. These are the most numerous in the more severe forms of inflammation, where they may give to the effusion a hemorrhagic character. Lastly, in inflammation of certain tissues, especially epithelial and endothelial structures, some of the cells met with in the effused liquid are derived from the proliferating elements of the inflamed tissue. The proportion of cells varies with the intensity and with the stage of the inflammation. The more intense the process the more abundant the emigration, and hence the more richly cellular the effusion. With regard to the stage of the inflammation—it may be stated generally that emigration is more abundant in the later than in the earlier periods, so that in the latter the effusion may be an almost clear liquid.

The prominence of effusion or exudation as a constituent part of

the inflammatory process will vary considerably according to the nature and anatomical character of the tissue inflamed. In non-vascular tissues, as cartilage and the cornea, exudation can only occur from the neighboring vessels, and hence the effusion is found outside the part. In dense organs, as the liver, testicles, and kidney, owing to the compactness of the structure, a large amount of effusion is impossible, and what there is, is so intermingled with the structural elements that it does not appear as an independent material, but simply causes some swelling of the organ. In the kidney it escapes into the urinary tubes, and so appears in the urine. The effusion is most abundant, and constitutes an important *visible* constituent of the inflammatory process, in inflammation of those organs which possess a lax structure and in which the vessels are but little supported—as the lungs, and in tissues which present a free surface—as mucous and serous membranes.

The absorption by the *lymphatics* from an inflamed tissue has been shown experimentally to be considerably increased. This increased absorption, as in the case of simple mechanical effusions, tends to prevent or to diminish the accumulation of liquid in the part. (See “Mechanical Hyperæmia.”)

III. ALTERATIONS IN THE NUTRITION OF THE INFLAMED TISSUE.—The remaining constituent of the inflammatory process consists in alterations in the nutrition of the elements of the inflamed tissue.

The question as to how far the cellular elements of the tissue participate in the process of inflammation is one which even in the present state of our knowledge, owing to the difficulties which beset the histological examination of inflamed structures, admits only of an incomplete answer. The subject has, for the most part, been investigated in the lower animals, in which inflammation has been artificially induced. In man, the study of the primary changes is difficult, owing to the fact that the process can rarely be observed in its earlier stages. These changes will be more fully described when considering inflammations of particular organs and tissues; it will be sufficient in the present place merely to indicate their general characters.

The alterations in nutrition which accompany inflammation are in certain tissues characterized by an exaltation of the nutritive functions of some of the cellular elements involved in the inflammatory process. This is evidenced by an increase in the activity of those elements which normally exhibit active movements, as the amoeboid

cells of connective tissue and of the cornea. Cells, which under normal circumstances undergo no alterations in form, and exhibit no

FIG. 74.



Amœboid Leucocytes. (v.
Recklinghausen.)

active movements, become active—sending out processes, and undergoing various alterations in shape. (Fig. 74.) This increase in the activity, and variation in the form of the cells, is usually accompanied by the growth of their protoplasm, and frequently by its division, or by vacuolation and endogenous development,

and thus by the formation of new cells. In many cases the protoplasm, as it increases in bulk, becomes cloudy and granular, so much so as frequently to completely obscure any nuclei which it may contain. This occurs especially in epithelial elements, and it constitutes the condition known as “*cloudy swelling*.” It is well seen in the glandular epithelium of the kidney in acute tubal nephritis. (See Figs. 117 and 118.)

A few years ago the cells of nearly all tissues were believed to exhibit these active changes in inflammation, and many of the young elements which abound in inflamed parts were regarded as the products of their proliferation. As our methods of histological investigation improve, however, and especially since the introduction of the chloride of gold process by Cohnheim, it has become increasingly obvious that the part which is played by the cells of the tissue in inflammation is much less than was formerly supposed; and that in most cases the young elements which infiltrate the inflamed structure are solely escaped leucocytes.

The physiological peculiarities of the cellular elements appear to influence very considerably their liability to undergo these active changes in inflammation. The cells in which active changes undoubtedly occur are those which are *normally* active, and in which growth and proliferation are associated with the maintenance of the tissue of which they are constituents. Such are epithelial elements. The activity of these is increased in the process of inflammation, and it is in inflammation of the skin, of mucous membranes, and of glandular structures, that cellular activity and proliferation are so constantly met with. The same is also true to a less extent of endothelium, as is exemplified in inflammations of serous membranes. In those cells, on the other hand, in which normally no active changes take place, as the fixed cells of connective tissue and of the cornea, and probably also those of cartilage, it is doubtful if any activity is manifested in

inflammation. The *age* of the cells probably also influences their tendency to become active, the younger being less stable and more prone to proliferate than the older elements.

Although the earlier alterations in the nutrition of the cellular elements are thus in some cases those of increased activity, the tissue changes in inflammation are, in the main, characterized by *impairment* of nutrition. The well-known effect of inflammation is to injure the part affected by it. This injurious influence is due to several causes. The initial injury which produces the vascular phenomena must, in many cases, damage the tissue outside the vessels before it can influence the vessels themselves. The most important interference with nutrition, however, is due to stagnation of the circulation, and to the infiltration of the tissue with the inflammatory products which have escaped from the bloodvessels. (See "Suppuration.") If the inflammatory process be of considerable intensity and stasis be induced in a wide area of the tissue, the nutrition may become completely arrested, and necrosis be the ultimate result. (See "Causes of Necrosis.") In inflammations of less intensity, the destruction of the tissue is less marked, the young cells which infiltrate it may undergo fatty degeneration and become absorbed, and the part thus recover more or less completely its former condition. In other cases, especially in the less severe forms of inflammation, many of the young cells undergo progressive changes and lead to the development of a permanent tissue, which is, however, for the most part, inferior in its organization to the parent structure. (See "Terminations of Inflammation.") This tendency of the new elements in inflammation to undergo progressive development will vary with the tissue involved, and with the intensity of the inflammation. The more intense the inflammation, the more abortive are the young cells, and the less is their tendency to form a permanent tissue. (See "Acute and Chronic Inflammations.")

In connective tissues, these changes in the cells are necessarily accompanied by changes in the intercellular substance. The latter are for the most part characterized by softening. In common connective tissue the fibres in the first place become swollen and less distinct, and ultimately they are completely destroyed; in cartilage the matrix softens and liquefies; in bone, the lime-salts are removed, the lamellæ disappear, and the osseous structure becomes converted into medullary tissue. Hence the destructive effects of the inflammatory process.

Having thus briefly described the succession of changes which occur in the process of inflammation, it remains to consider in what way these result from the injury of tissue, and how far a causal relation subsists between them.¹

The first apparent change which follows the injury of the tissue consists in the dilatation of the bloodvessels, and in an *acceleration* of the flow of blood. This acceleration of the circulation which, as has been said, does not invariably occur, is precisely similar to that which results from injury of a sensory nerve (see "Active Hyperæmia"); and in a previous edition of this work it was stated that the primary vascular phenomena in inflammation were probably due to injury of the sensory nerves of the part, although such injury could not explain the subsequent and essential retardation of the blood-flow. The more recent investigations of Cohnheim, however, which have been already quoted, render it necessary that this statement should be considerably modified. Cohnheim produced precisely the same phenomena in the tongue of the frog, after everything had been cut through with the exception of the lingual artery and vein, as those which occur in the intact animal; and also, in another case, after complete destruction of the brain, medulla, and spinal cord; and he considers that the vascular dilatation and accelerated blood-flow are due to the *direct* influence of the injurious agent upon the *walls of the bloodvessels*, and are quite independent of nervous influence. These experiments therefore appear to prove conclusively that the initial injury of the bloodvessels is not necessarily reflex, although they do not exclude the possibility that it may be so under certain circumstances.

The *retardation* of the blood-stream which so quickly succeeds its acceleration, the essential and sometimes primary phenomenon of inflammation, differs so much from all non-inflammatory forms of hyperæmia, that its explanation has ever engaged the attention of pathologists. Abnormal conditions of the blood, of the tissues, of the walls of the bloodvessels, and of innervation, have at different times been supposed to account for it, but it is now satisfactorily established that it is due to some alteration in the properties of the walls of the bloodvessels through which the blood passes. That the retardation and ultimate stagnation of the blood-stream in acute in-

¹ The following conclusions are in the main those arrived at by Professors Stricker and Burdon Sanderson.—*Holmes's System of Surgery*, vol. v. See also Lectures on the "Pathology of the Process of Inflammation," by Professor Sanderson.—*Lancet*, vol. i. 1876.

flammation is due to alterations in the walls of the bloodvessels and not to changes in the blood itself, was first shown by Mr. Lister.¹ Mr. Lister proved experimentally that the blood removed from an inflamed part did not differ in the tendency of the red blood-corpuscles to cohere to one another from normal blood; and he concluded that the accumulation of the red corpuscles in inflamed tissues, and their adhesion to one another and to the walls of the vessels, was owing to their natural tendency to cohere together when in *abnormal* circumstances, such as occurs after their removal from the body; and that this cohesion in inflammation which leads to stasis was due to impaired vitality of the walls of the bloodvessels. This conclusion of Mr. Lister has been verified by more recent investigations. Ryneck has shown that stasis may be produced in the web of a frog, in which milk or defibrinated blood has been injected in place of the normal blood; and also that in vessels, the vitality of which has been completely destroyed by the injection of poisonous metallic substances, no stasis can be produced.² The investigations of Prof. Cohnheim are still more conclusive. Cohnheim ligatured the ear of a rabbit at its base with the exception of the median artery and vein, and emptied the vessels of their blood by the injection of a weak saline solution. He then injected into the emptied vessels various irritating solutions, and on again allowing the blood to flow through the thus injured vessels all the phenomena of inflammation ensued.³ His experiments, already described when speaking of local anæmia, the result of which was to show that if the circulation in any organ (as the ear of the rabbit) be completely arrested for a sufficient length of time by the simultaneous occlusion of the arteries and veins, and then the blood be again allowed to circulate, dilatation of the vessels, hyperæmia, stagnation, exudation, and all the phenomena of inflammation take place in the part, also prove that an injury to the walls of the bloodvessels caused by depriving them, for some time, of arterial blood, is followed by retardation of the circulation and the subsequent phenomena of inflammation. The results of these experiments appear to be conclusive, and show that the retardation and ultimate stagnation of the blood-stream, in inflammation, are owing to some impair-

¹ "On the Early Stages of Inflammation."—*Philosoph. Trans.*, 1858.

² Ryneck, "Zur Kenntniss der Stase des Blutes in den Gefassen Entzündeter Theile."—Rollet's *Untersuch. aus dem Institute für Phys. u. Histol. in Graz*.

³ "Neue Untersuchungen über die Entzündung," Cohnheim, 1873.

ment of the vital properties of the walls of the bloodvessels with which the circulating blood comes into contact.

In explanation of the phenomena of *exudation* and *emigration*, which take place coincidently with the retardation of the blood-stream, it may be stated in the first place that these are not due to any increased blood-pressure such as exists and accounts for the exudation in mechanical hyperæmia, inasmuch as the pressure within the vessels of an inflamed area is less than natural. Neither can they be due to the enlargement of stomata which have been supposed to exist between the endothelium, because if such openings existed the unaltered blood would escape, and not certain constituents of it only; and a similar escape would occur in conditions as active hyperæmia. From the experimental investigations which have been described, there can be no doubt that these two phenomena of inflammation are, like the dilatation of the vessels and retardation of the circulation with which they are associated, due to some *alteration in the vital properties of the walls of the bloodvessels*, an alteration possibly of a chemical nature, but at all events, one not accompanied by any structural change recognizable by our present methods of observation. This alteration increases the resistance between the blood and vessels, and so impedes the circulation, and also permits the transudation of constituents of the blood which normal vessels retain. The causes of this alteration may be very various, but they all lead to similar results, and if their injurious influence be sufficiently pronounced, they may completely destroy the vitality of the vessel. When this occurs, as was seen in the chapter on thrombosis, the blood coagulates, and we pass from the confines of inflammation into those of necrosis.

The remaining constituent of the inflammatory process—the alteration in the nutrition of the inflamed tissue—succeeds the changes in the circulation and the exudation. Respecting the cause of the increased nutritive activity of the cellular elements which characterizes inflammation in certain tissues—it is probable that this is, for the most part, the result of the stimulation of the cells by the liquor sanguinis exuded from the bloodvessels, and the increased supply of nutriment with which they are surrounded. (See “Nutrition Increased.”) The impairment of nutrition produced by inflammation is due partly to the stagnation of the blood, and partly to the injurious influence of the products which escape from the bloodvessels. (See “Suppuration.”)

SUPPURATION.—Suppuration, and the formation of abscess, is a very frequent result of the inflammatory process; it occurs much more frequently, however, in some inflammations than in others. As a rule it may be stated that the more intense the inflammation the more abundant is the formation of pus.

The essential constituents of pus are cells and a liquid in which they are suspended. The liquid has an alkaline reaction and closely resembles the liquor sanguinis. It contains various kinds of albumen, fatty matters, and inorganic substances. The cells, or *pus-corpuscles* (leucocytes), are indistinguishable from the white corpuscles of the blood. As seen after death, they are spherical, spheroidal, or irregular-shaped, semi-transparent bodies, from $\frac{1}{2500}$ th to $\frac{1}{3500}$ th of an inch in diameter, containing a varying number of granules, and usually one or more distinct nuclei. (Fig. 75.)

The addition of dilute acetic acid causes the cells to swell up; they become more spherical and transparent, and the nuclei are rendered more apparent. The size of the corpuscles and nuclei, and the number of the granules, present manifold variations. Pus-corpuscles, like white blood-corpuscles, lymph-corpuscles, and many other young cell-forms—all of which are included under the common term of *leucocytes*—are masses of contractile protoplasm. They possess the power of spontaneous movement, and when living undergo continuous alterations in form, and migrate in the tissues. (See Fig. 74.) They may also multiply.

The mode of origin of pus has been the subject of much controversy. The liquid ingredient proceeds directly or indirectly from the blood, it is the exuded liquor sanguinis: about this there is no dispute. The difference of opinion which has existed is respecting the origin of the formed elements. Without discussing obsolete theories, it must now be admitted that there are *two* sources from which the cells of pus may be derived—one from the *blood*, and the other from the *inflamed tissues*.

It has been seen that in the process of inflammation innumerable white blood-corpuscles pass out of the vessels into the surrounding tissues, and as these are indistinguishable from pus-corpuscles, it must be conceded that one mode of origin of pus is from the blood. Further, the white blood-corpuscles may multiply, and it is probable that by this means the production of pus may be greatly increased.

The other source from which the cells of pus are derived is from

FIG. 75.



Pus-corpuscles as seen after death.—a. Before, b. after, the addition of dilute acetic acid. X 400.

the cellular elements of the inflamed tissue. In certain tissues, as has been seen—especially in the epithelial and endothelial tissues—the cells are the seat of active changes in inflammation; they may multiply and form new cells, and the more intense the inflammation, the more lowly organized are the newly-formed elements, and the less is their tendency to form a permanent tissue. Some of these newly-formed cells constitute pus-corpuscles. These, in this case, must be regarded as young elements resulting from the proliferation of the tissue, which are of low vitality, and soon perish.

Although the formed elements of pus may thus be derived both from the blood and from the inflamed tissue, there can be no doubt that the former is their principal source, and that they are in the main migrated blood-corpuscles. In the earlier stages of the inflammatory process, they are mostly, if not all, emigrants; but in the later stages it must be admitted that they may also, in certain tissues, be derived from the cells of the inflamed part.

The blood being the principal source of pus, it is evident that the more abundant the escape of blood-corpuscles, the greater will be the formation of this product, and hence the greater its tendency to collect so as to form an abscess. It is consequently in those inflammations which are the most *concentrated* and the most *intense*—provided that the injury be not sufficiently severe to cause complete stasis—that the formation of pus is most abundant. The greater the injury sustained by the walls of the bloodvessels, the more readily will the blood-corpuscles penetrate them, and hence the more abundant will be the formation of pus. In inflammations of less intensity the escape of blood-corpuscles is less abundant, so that pus is not produced in sufficient quantities to cause its collection in the form of an abscess, and the corpuscles may merely infiltrate the part in such few numbers as to require for their recognition the use of the microscope.

Pus exercises a most injurious influence upon the surrounding tissues. The pus-corpuscles appear to be endowed with the power of absorbing the tissues with which they come in contact, or, at all events, of causing their liquefaction. Hence the softening and disintegration of the tissues which constitute such a destructive element in intense inflammations.

Pus which has remained for any length of time in the tissues undergoes certain changes. Its elements may undergo fatty metamorphosis, and thus be rendered capable of absorption. If pus is long confined in a closed cavity, its liquid portions may become absorbed, and its

cells atrophy, so that it gradually dries up into a caseous mass, which may subsequently become calcified.

VARIETIES OF INFLAMMATION.—1. The most important variations in inflammation are due to the amount of alteration in the walls of the bloodvessels, in other words, to the *intensity* of the inflammatory process. The extent to which the vessels are altered depends upon the severity of the initial injury, and the degree of susceptibility to its injurious influence; the vascular, like other tissues, being much more easily influenced injuriously in some individuals and in some states of health than in others. In speaking therefore of the intensity of an inflammation, it must be borne in mind that it comprises these two factors. From what has been already stated it will be obvious that upon the intensity of an inflammatory process will depend the extent and character of the exudation from the vessels—the greater the intensity, the more abundant, the more highly albuminous, and the more richly cellular the exuded liquids. Hence it is in inflammations of considerable intensity that the vascular phenomena are often so pronounced, the formation of pus so abundant, and the softening and disintegration of the tissues so considerable. Such inflammations, inasmuch as the action of the injury which produces them is for the most part of short duration, are sometimes designated *acute* inflammation.

In inflammation of less intensity the vascular phenomena are less marked, the exudation is less albuminous, and the formation of pus is less abundant. It is in many of these less intense and more chronic forms of inflammation that new growth occupies a prominent place. The new growth consists in the main of an increase of the connective tissue around the bloodvessels, although in certain tissues, especially epithelial and glandular structures, this is associated with an increase of the epithelial elements. It appears to me to be probably true—that the less intense the inflammatory process, the more do the resulting textural changes tend to be limited to the connective tissue which is immediately adjacent to the bloodvessels, whereas in inflammations of somewhat greater intensity the epithelial elements become involved. This is seen, for example, in inflammation of the kidneys and mucous membranes. In the former, the least severe forms of inflammation are characterized histologically by an increase in the connective tissue around the bloodvessels (see “Interstitial Nephritis”);

whilst in inflammations of somewhat greater intensity, the prominent textural change consists in swelling or proliferation of the epithelium within the tubules. (See "Tubal Nephritis.") In mucous membranes, also, the more severe inflammations are attended by epithelial proliferation, the less intense and more chronic by changes in the submucous connective tissue. The tendency of the textural changes resulting from the least severe forms of inflammation to be limited to the connective tissue immediately adjacent to the bloodvessels, gives to these inflammations certain peculiarities. The new tissue—consisting in the earlier stages mainly of small round cells, but ultimately becoming developed into a more or less completely fibrillated structure (an adenoid or fibrous tissue)—leads to an *induration* of the organ in which it is situated, and very often, to the subsequent atrophy and retrogressive metamorphosis of its other histological elements. These changes will be more fully considered when treating of inflammation of the individual organs and tissues. (See "Inflammation of Common Connective Tissue," "Cirrhosis of the Liver," etc.) These least intense forms of inflammation, inasmuch as the injury which produces them is not only of slight severity, but is usually also prolonged and intermittent in its action, are often known as *chronic* inflammations.

2. Inflammations vary considerably in the character of the effusions to which they give rise, hence they are *serous*, *fibrinous*, and *suppurative* inflammations. These differences are obviously closely connected with differences in the intensity of the inflammatory process.

A *serous* effusion is one containing but little albumen and a few blood-corpuscles, and consequently having but little tendency to coagulate. Such effusions occur in inflammations of slight intensity, in which the alteration in the walls of the bloodvessels is only sufficient to allow the more watery constituents of the blood to escape. In more intense inflammations also, where the emigration of blood-corpuscles is not fully established, as in the earlier stages of the process, and when the injury to the vessels, although severe, is rapid and transient in its action, as that caused by heat and blistering agents, the effusion is often a clear and only slightly coagulable liquid. Lastly, in an impoverished state of the blood, especially where the albumen is diminished, an inflammatory exudation, even when the process is of considerable intensity, is liable to be of a serous or very imperfectly fibrinous character.

A *fibrinous* effusion is more richly albuminous than the preceding, contains more blood-corpuscles, and consequently has a much greater

tendency to coagulate ; so that layers of fibrin are found adherent to the inflamed surface. Fibrinous effusions are usually due to a graver alteration in the walls of the vessels than serous—an alteration which allows more of the constituents of the blood to escape. As just stated, they may not occur in impoverished conditions of the blood, even though the inflammation be of great intensity.

A *suppurative* effusion contains so many blood-corpuscles that it is distinctly purulent. (See “Suppuration.”) This abundant escape of leucocytes is due to an inflammation of considerable intensity, to one in which the alteration in the walls of the vessels is more marked, and the injurious influence is for the most part more prolonged than that which permits the escape of a less corpuscular liquid. The suppuration is often preceded by a serous or fibrinous effusion, the blood-corpuscles, as already stated, escaping at a later period in the process than the liquor sanguinis.

3. One of the most important divisions of inflammation is into *infective* and *non-infective*. An infective inflammation is one of the products which possess infective properties, owing to which the substances which are absorbed from the inflamed part tend to cause secondary inflammations of the tissues with which they come into contact. This infective property has in the first place a local influence, causing inflammation in the tissues immediately adjacent to the part primarily affected:—infective inflammations have thus a tendency to spread. The infective substances being absorbed by the bloodvessels and lymphatics then tend to cause inflammation in distant tissues:—thus the process becomes disseminated. What it is that causes the products of an inflammatory process thus to become infective will be considered more fully in the chapter on Septicæmia and Pyæmia. It will be sufficient here to state that in all infective inflammations the formation of the infective substance appears to be due to the presence of minute organisms, these organisms in the ordinary non-specific infective inflammations being the common septic bacteria.

4. Inflammations have received different names, according to the *nature* of the injury upon which they depend. Those inflammations which result from external injuries, mechanical or chemical violence, are called *traumatic*. Inflammations in which the nature of the injury is not obvious, are usually called *idiopathic*. The nature of the injury may give to the inflammatory process certain peculiarities. The contagium of smallpox, for example, gives rise to inflammation of the skin, constituting the “rash;” that of syphilis, to certain in-

inflammations of the skin, mucous membranes, and other tissues; and that of typhoid fever, to inflammation of the intestinal lymphatic structures. In all these and numerous similar cases, the nature of the injury impresses upon the inflammation certain peculiarities, and in so far as the former is specific, the latter may be called *specific* inflammations. Lastly, inflammatory processes may be modified by the existence of certain *constitutional* peculiarities. This is the case especially in Scrofula.

TERMINATIONS OF INFLAMMATION.—1. *Resolution*.—This, the most frequent and most favorable termination of inflammation, consists in the cessation of the process and the restoration of the part to health. In order for this to occur, it is necessary, in the first place, that the injurious influence, whatever it may be, should be removed. This being done, there must be a restoration of the walls of the bloodvessels to their normal condition, in order that the abnormal transudation may be arrested. This restoration will obviously be more easily effected in the earlier than in the more advanced stages of the inflammatory process. A normal condition of the walls of the bloodvessels is dependent upon the proper circulation of the blood through them and the vaso vasorum. Whatever, therefore, favors the re-establishment of the circulation in the inflamed area will, as pointed out by Cohnheim, favor resolution.

Another necessary element in resolution is the removal of the inflammatory products. This is effected mainly by the lymphatics, the effused liquid and blood-corpuscles passing into the lymphatic channels. After the restoration of the circulation, absorption is also carried on to some extent by the bloodvessels. In the latter stages of the process any unabsorbed blood-corpuscles or fibrin undergo fatty degeneration, and thus the complete removal of the inflammatory products is much facilitated. (See “Gray Hepatization.”)

It will thus be obvious that all those conditions which interfere with the lymphatic or vascular circulation, such as the pressure exercised by large quantities of effusion in a serous cavity, or by a richly cellular exudation in a lymphatic gland, must retard resolution. (See “Caseation” and “Scrofulous Inflammation.”) Interference with the lymphatic circulation tends especially to prevent absorption, interference with the circulation in the bloodvessels to prevent that

restoration of those vessels to a normal condition which is necessary in order to arrest the continued transudation.

2. *Necrosis*.—Inflammation may terminate in the death of the inflamed tissue. This result is liable to occur if the initial injury is of considerable severity and the duration of its action is prolonged. Such injuries, by completely destroying the vitality of the vessels in that area where their injurious influence is the most marked, cause thrombosis; and this, together with the interference with the circulation due to exudation from the unthrombosed vessels, lead to the death of more or less of the affected part.

Considerable impairment of the vitality of a tissue also renders it, when inflamed, very liable to become necrotic; hence the frequency with which inflammations in the aged and debilitated terminate in gangrene. (See “Senile Gangrene.”) This liability is partly due, as already explained, to the weakened vessels being abnormally susceptible to the injurious influence, so that very slight injuries may cause intense inflammations; and partly to the feebleness of the circulating forces, and consequent inability to restore the circulation in the inflamed area.

3. *New Growth*.—The development of new tissue has already been alluded to as a result of many of the less intense inflammations. In order for this “productive” inflammation to occur, the inflammatory process must not be of sufficient intensity to cause abundant pus-formation, but yet intense enough, and the blood of a sufficiently healthy character, to lead to a fibrinous exudation and the escape of a certain number of leucocytes. It is from a fibrinous effusion containing white blood-corpuscles—the so-called plastic lymph—that the new tissue is produced. The new tissue is invariably a connective tissue, and its development will be considered when speaking of inflammation of connective tissue. It will be sufficient here to state that the process consists in the development of some of the escaped leucocytes into larger cells, the formation of numerous new blood-vessels, the fibrillation of the growth, and its ultimate development into a vascular connective tissue, which subsequently becomes less vascular and tends to contract. This productive inflammation occurs in the union of wounds, the healing of ulcers, in chronic inflammation of organs, etc. (See “Inflammation of Common Connective Tissue.”)

CHAPTER XXX.

SCROFULOUS INFLAMMATION.

THE process of inflammation when occurring in the scrofulous usually presents certain peculiarities.

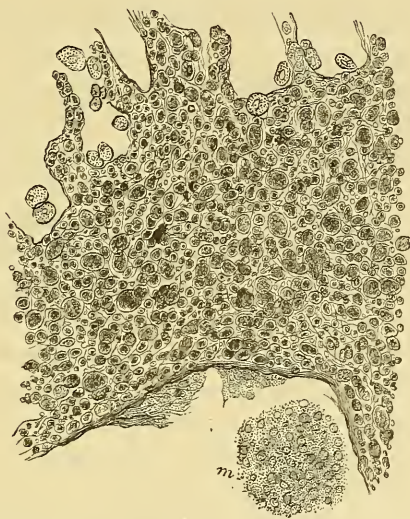
The constitutional condition known as scrofula—a condition usually inherited but often acquired—is characterized by certain pathological tendencies. Of these the most important is an abnormal susceptibility of certain tissues to injury, and a peculiarity in the products and in the course of the inflammation which the injury induces. This susceptibility, more or less general, is commonly most marked in the mucous membranes and in the lymphatic glands, although the skin, bones, and joints are frequently affected. The part, however, which is the most prone to suffer varies considerably in different cases.

Not only is there this susceptibility to inflammation, but the inflammatory process tends to be exceedingly protracted; it is very readily reinduced, and the alterations produced in the part differ from those caused by inflammation in healthy persons. When inflammation occurs in a healthy individual, if it does not cause the death of the part, the inflammatory products either become absorbed, or the process leads to suppuration, or to the formation of a vascularized connective tissue. In scrofulous inflammation the absorption of the inflammatory products is very much less readily effected: they tend to *infiltrate* and *accumulate* in the tissue, where by their pressure they interfere with the circulation, and so lead to retrogressive and *caseous* changes. There is but little or no tendency to the development of new bloodvessels, and hence there is no organization of the new growth.

These peculiarities of inflammation in scrofulous subjects are to be in great measure ascribed to that inherent low vitality of the tissues which obtains in this disease, and also to certain peculiarities in the histology of the inflammatory products. Virchow long ago pointed out the richly cellular character of the products of scrofulous inflammation, the tendency of the cells to infiltrate the tissue, and the extreme tardiness with which the infiltration becomes absorbed. Quite

recently Professor Rindfleisch has stated that these cells are, for the most part, *larger* than those met with in healthy inflammations; and that this being the case, their removal by passage into the lymphatics is less readily effected.¹ In tubercle, the close relation of which to scrofulous lesions is well known, the existence of large cell-forms is almost constant, and their pathological significance in both these allied products will be more fully considered when speaking of tuberculosis. (See "Tubercle and Acute Tuberculosis.") This largeness of many of the young cells in scrofulous inflammation, and their marked tendency to infiltrate and accumulate is well shown in the accompanying drawing (Fig. 76).

FIG. 76.



Scrofulous Inflammation of a Bronchus.—Section of a small bronchus of a markedly scrofulous child, the subject of bronchitis, which terminated in miliary tuberculosis. The deeper structures of the bronchial wall are seen to be extensively infiltrated with cells, most of which are *larger* than those met with in the less extensive infiltration of healthy inflammation. The infiltration extends to and invades the walls of the adjacent alveoli, which are seen at the upper part of the drawing. The cavity of the bronchus contains a little mucus, *m*. $\times 200$, reduced $\frac{1}{2}$.

These histological peculiarities of the products of scrofulous inflammations not only lead to an extensive and obstinate infiltration of the affected tissues, but, as insisted upon by Rindfleisch, they must in the parenchyma of organs, as in the glands and viscera, cause, by the

¹ Ziemssen's "Cyclopædia of Practical Medicine," vol. v. Article, Chronic and Acute Tuberculosis, by Rindfleisch.

pressure they exercise, more or less obstruction of the bloodvessels, and so interfere with the vascular supply. To this interference with the vascular supply, and to the inherent low vitality of the cellular elements, is to be mainly ascribed the retrograde changes and *caseous metamorphosis* which are so characteristic of scrofulous lesions.

CHAPTER XXXI.

TUBERCLE AND ACUTE TUBERCULOSIS.

By acute tuberculosis is understood a general infective disease, which is characterized anatomically by the occurrence of numerous minute nodular lesions more or less generally disseminated in the various organs and tissues. The generally disseminated nodular lesions, which are characteristic of the disease, appear to be inflammatory growths, resulting from the distribution of infective materials (probably minute particles), by means of the bloodvessels or lymphatics from some primary inflammatory product. They are, therefore, the anatomical results of an infective inflammatory process and they constitute what have long been known as *miliary tubercles*.

General Pathology of Acute Tuberculosis.—Our knowledge of acute tuberculosis and of its anatomical result—*tubercle*, has until recently been involved in obscurity; but at the present time—owing in great measure to scientific experimental research—it may be regarded as being much more complete. According to the older doctrines, which were based upon the teaching of Laennec, tubercle was looked upon as a specific non-inflammatory growth which originated spontaneously in the tissues. Further, this new growth was characterized by the regular succession of changes which it invariably underwent—it was first gray and translucent, then became opaque, and ultimately caseous. Hence in its earlier stages it was known as *gray*, in its latter as *yellow tubercle*. Caseous metamorphosis was held to be such a distinguishing peculiarity of the growth, that all caseous masses were regarded as tubercular, and the term “tubercle” came to be applied indiscriminately to all pathological products which

had undergone this form of degeneration, and which in their color and consistence somewhat resembled soft cheese. Caseation, however, as already stated, although most frequent in tuberculous and scrofulous lesions, is a common result of the retrograde metamorphosis of many growths which are destitute of or contain but few blood-vessels, and which consist of closely crowded cellular elements. (See "Caseation.") For this much wider extension of the pathological significance of caseous degeneration we are mainly indebted to Professor Virchow.¹

The infective nature of acute tuberculosis was first promulgated about twenty years ago by Buhl, who stated that in the majority of cases of this disease indurated masses which had become caseous existed in some part of the body, and that to the absorption of substances from these infective centres the general development of the tubercle was owing. He further stated that in those cases in which the tubercles were confined even to limited portions of a single organ, they were also secondary to caseous lesions. Buhl's theory, therefore, implied that the origin of the infective substances was necessarily associated with caseous metamorphosis of the primary inflammatory induration. A modification of this view of the nature of the infecting lesion has since been rendered necessary, both by the results of post-mortem observations, and also by those which have been obtained from the artificial production of tuberculosis in the lower animals.

The experimental investigation of acute tuberculosis was commenced by Villemin in 1865, and subsequently followed out by Burdon Sanderson, Wilson Fox, Cohnheim, Klebs, and others. The methods of investigation consisted either in the inoculation of various inflammatory products—for the most part products of *chronic* inflammations (caseous or not caseous), or in the production of a local inflammatory induration by the introduction of setons and of other foreign bodies beneath the skin. Of inflammatory products Dr. Sanderson found that none proved so active as that obtained from the indurated lymphatic glands of an animal already suffering from the disease. In both cases, after a certain lapse of time, disseminated inflammatory lesions were produced in various organs and tissues—lesions which presented a special tendency to become caseous at their centres. It was also found that the distribution of these lesions varied according

¹ For further information on the history of "tubercle," the reader is referred to the commencement of the chapter on "Pulmonary Phthisis."

as the infective materials were introduced into the bloodvessels or lymphatics, clearly proving that they resulted from the dissemination of infective substances by means of the blood and lymph streams. The result of these experiments therefore show, in the first place, that caseation of an inflammatory product is not necessary in order for it to constitute an infective focus; and, secondly, that the development of the general tuberculosis is not due to anything specific in the substances inoculated, but that the products of various inflammatory processes (for the most part of inflammation of slight intensity), may constitute the infective agents.

The lesions produced, however, in artificial tuberculosis differ somewhat from those met with in the natural disease as it occurs in man. They differ both in their anatomical distribution, and, to a less extent, in their pathological tendencies. The differences in anatomical distribution are principally confined to the brain and lungs. The brain, which is so frequently affected in the natural disease in man, is rarely so in artificial tuberculosis. In the lungs, the first structural changes which take place in artificial tuberculosis are stated by Dr. Klein to consist in the development of adenoid tissue around the perivascular lymphatics, the implication of the alveoli being only a secondary part of the process.¹ In the natural disease in man, on the other hand, the changes commence in the alveoli themselves. Respecting differences in their pathological tendencies—it is to be remarked that caseation occurs much more extensively in the lesions artificially induced than in man. In the former, also, diffused tracts of consolidation are more frequently associated with the miliary lesions, and they may even constitute the predominant structural changes. These differences, however, are probably to be regarded as resulting from differences in the intensity of the infective process, and from peculiarities in the morbid tendencies of the tissues involved, and not as any evidence of a want of analogy in the pathology of the two diseases.

Passing on to consider acute tuberculosis as it is met with in man, it must in the first place be stated that it occurs most frequently in those who are *scrofulous*, and one or more masses of inflammatory induration which have become *caseous* are, in the great majority of cases, to be found in some parts of the body after death; sometimes in the lungs, sometimes in the bronchial glands, sometimes in the

¹ "On the Lymphatic System of the Lungs," by Dr. E. Klein: *Proceedings of the Royal Society*, No. 149, 1874.

glands of the mesentery, etc. Caseous metamorphosis, as was seen in the preceding chapter, is exceedingly common in scrofulous inflammation, owing to the marked cellular infiltration and consequent anæmia which characterize the process; and *it is these products of scrofulous inflammation which are the most common cause of acute tuberculosis*. Much less frequently cases of acute tuberculosis are met with, in which there exists some inflammatory lesion which is not caseous, as a simple induration, an inflamed bone, or an ulcerated mucous membrane; whilst in exceedingly rare cases it is stated that no such products of a previous inflammatory process has been discoverable.

The results of post-mortem observations of the natural disease thus appear to justify the same conclusions respecting the nature of the infective substances as those derived from the experimental investigation of the disease in the lower animals, and in a man also it must therefore be regarded as in the highest degree probable that any inflammatory product may, under certain circumstances, give rise to a tuberculous process, and that although caseation of the product is most frequent, it is not essential in order for it to constitute an infective focus. Why such inflammatory products should in some cases be infective, whilst in others they remain inert, we are unable certainly to explain. In attempting to answer this question, it must be remembered that such product may *accidentally* become placed in direct communication with the vascular or lymphatic systems; and also that infective substances are much more liable to produce results in some constitutions and in some conditions than in others. It is also possible that the infective properties of an inflammatory product may be determined by atmospheric influence or by the presence of minute organisms. (See "Septicæmia.")

Whilst acute tuberculosis is thus an infective disease, it is an infective disease of a special kind. In the first place, the infective substances derived from the infective focus—which are probably minute particles—not only exercise their injurious influence over areas of tissue which are for the most part exceedingly small (hence the miliary characters of the lesions), but the injury they inflict is of comparatively slight severity. The principal result of their dissemination is consequently to cause a textural change—a new growth of tissue at the seat of the injury. (See "Chronic Inflammations.") In this respect this disease presents a marked contrast to one with which it is closely allied—pyæmia, in which the severity of the injury

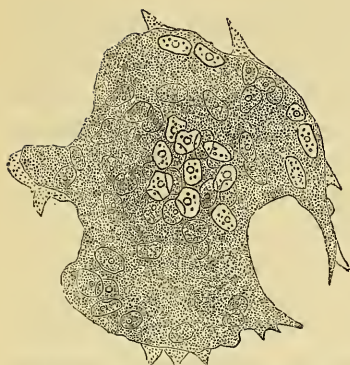
produced by the infective particles is much greater, and gives rise to the formation of abscesses. (See "Pyæmia.") In pyæmia the intensity of the disseminated inflammatory processes is considerable, and the course of the disease is usually acute, whilst in acute tuberculosis the inflammatory processes are much less severe, and the disease tends to run a more chronic course.

HISTOLOGY OF TUBERCLE.—The miliary lesions in acute tuberculosis, although presenting certain differences according to their age, and to the nature of the tissue in which they originate, are tolerably uniform in their histological characters. Their most marked feature is the prominent place which large multinucleated masses of protoplasm—the so-called giant cells—occupies in their constitution. These large cells which somewhat resemble the myeloid cells met with in sarcomatous tumors, etc., were long ago alluded to by Virchow, Wagner, and others, but it is only during recent years, mainly owing to the researches of Oscar Schüppel and Langhans, that they have come to occupy a prominent place in the histology of tubercle.

The most characteristic features of these multinucleated cells are their large size, the number of their nuclei, and the irregularity of their outline. Some of the larger ones measure as much as $\frac{1}{200}$ inch in diameter. They possess no limiting membrane, but are simple masses of protoplasm, containing numerous round or roundly-oval nuclei, each inclosing a bright nucleolus. (Figs. 77, 78, and 79.) As many as forty nuclei may occasionally be counted in a single cell. Some of them are much smaller, and contain only three or four nuclei. Four or five, or even more, of these multinucleated masses are sometimes found in a single tuberculous nodule. Many of these large cells possess long branched processes, in connection with which, and evidently originating from them, are smaller protoplasmic masses, also nucleated and branched. (See Figs. 78 and 79.) The meshes between the branched cells are, according to Schüppel, filled with epithelial-like elements. These elements I have failed to observe, and the meshes I have either found empty, or containing a few lymphoid cells. (Fig. 79.) It would thus appear that the original protoplasmic mass gives origin to a network of large branched cells.

With regard to the histological elements from which the giant cells originate—this varies. In the lung, Dr. Klein states that they are derived from the alveolar epithelium. They may also probably originate from the cells of connective tissue, and from the endothelium of the bloodvessels and lymphatics. Their formation takes place either

FIG. 77.



A Multinucleated Cell from the Lung in a Case of Chronic Phthisis.—Showing the large number of nuclei with bright nucleoli. $\times 400$.

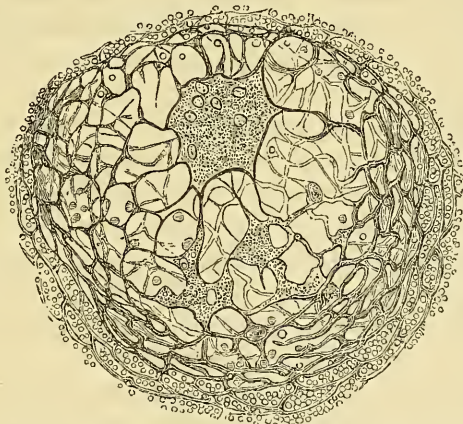
FIG. 78.



A Multinucleated Cell from the Lung in a Case of Chronic Phthisis.—Showing the long branched processes, which are continuous with the reticulum of the surrounding indurated growth. Some of the processes are in connection with smaller nucleated elements. $\times 200$.

by the fusion of two or more cells, or by the excessive development of one cell. In the latter case, the cell increases in size and its nuclei

FIG. 79.



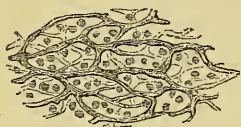
Multinucleated and Branched Cells from a firm Gray Miliary Tubercle of the Lung in a Case of Acute Tuberculosis.—Wide meshes are seen in the immediate vicinity of the cells inclosing a few lymphoid elements. The branched processes are directly continuous with the adenoid reticulum of the tubercle. $\times 200$.

multiply, but here the process of development ceases—there is no subsequent division of the cell.

Associated with, and surrounding the giant cell and its branches,

is a small-celled adenoid-like structure. (Fig. 79.) This small-celled structure, which usually contributes largely to the formation of the tubercle, somewhat resembles that of an indurated lymphatic gland, which is commonly known as adenoid tissue. A similar structure, as has already been stated, is also met with in chronic inflammations of the liver, lungs, and other organs. (See "Chronic Inflammations.") It consists, in the main, of lymphoid cells, which are either separated from one another by fine bands of homogeneous transparent-looking material, or by a more or less distinctly fibrillated,

FIG. 80.



A portion of a Gray Miliary Tubercle of the Lung.
—Showing the adenoid-like structure met with in large portions of these nodules. \times 200.

and sometimes nucleated reticulum, within the meshes of which the cells are grouped. (Fig. 80.) This reticulum is sometimes dense and well marked, whilst in other cases it is much less prominent. In addition to the small lymphoid cells there are often seen some rather larger cells containing one, and, in some cases, two nuclei. (See "Scrofulous Inflammation," Fig. 76.)

An elementary tubercle thus consists of a giant-cell reticulum surrounded by, and in direct histological continuity with, a varying sized zone of small-celled tissue. This is well shown in Fig. 79. (See also Fig. 83.) The larger tuberculous nodules consist of several of these giant-cell systems. (See Fig. 89.)

Although the above characters of tubercle are to be observed in successful preparations and in certain stages of the tuberculous growth, many of them will often be found wanting. The nuclei and processes of the giant-cells will not always be seen, and the cells often appear simply as yellowish, somewhat granular masses in which neither nuclei nor processes are visible. In this imperfect state they are to be found in tuberculous nodules from all organs in which tubercle is met with.

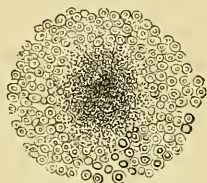
It remains to speak of the bloodvessels of tubercle. The vessels of the tissue in which the nodule originates gradually become obliterated in the process of its growth, and there is no new formation of vessels, such as takes place in more highly developed inflammatory tissue. (See "Inflammation of Common Connective Tissue.") The tubercle is therefore, except in the earliest stages of its development, non-vascular. (See "Scrofulous Inflammation.")

Although the structure which has been described is that most com-

monly met with, it must be borne in mind that all tuberculous lesions are not thus constituted. When treating of the changes in the several organs, it will be seen that the precise histological constitution of the nodules varies somewhat, according to the characters of the tissue in which they originate. In the lung, for example, many of them consist largely of accumulations of epithelial cells within the pulmonary alveoli.

Secondary Changes.—Tubercle invariably undergoes more or less retrograde metamorphosis, although the extent of this varies considerably, and in some cases the nodules may become developed into an imperfect fibroid structure. The occurrence of retrograde metamorphosis is mainly owing to the obliteration of the bloodvessels which accompanies the growth of the lesions. The change commences in the centre of the nodule, this being the part first developed, and consequently that which is the furthest removed from vascular supply. The nodule breaks down into a granular fatty débris, so that its central portions soon become opaque and yellowish. (Fig. 81.) In some cases the process of disintegration is rapid, whilst in others it is more gradual. It is usually most marked in the larger and more diffused lesions, and hence it is these lesions which are most commonly of a yellow color and soft consistence ("yellow tubercle"). In other cases the retrograde change is less marked, the reticulum of the nodule becomes denser and more fibroid, and although the imperfect fibroid tissue usually ultimately undergoes in its central parts more or less fatty metamorphosis, the nodule may remain as a firm fibroid mass.¹ This occurs more especially in the smaller lesions. The extent and rapidity of the retrograde change depends, I believe, partly upon the intensity of the infective process, and partly upon constitutional conditions. The existence of scrofula favors retrograde changes in tuberculous lesions as it does in all inflammatory products, and it is in those who are markedly scrofulous that tubercle undergoes the most rapid degeneration. (See "Scrofulous Inflammation.") These changes will also be influenced by the intensity of the infective pro-

FIG. 81.



One of the Gray Nodules from the Lung in a Case of Acute Tuberculosis, which is becoming opaque and soft in the centre. (Diagrammatic.)

¹ Dr. Klein states (*loc. cit.*) that the large multinucleated cells undergo a fibroid transformation, and become converted into a dense feltwork of fibrillar tissue, which tissue gradually dies away and becomes caseous.

cess. The more intense the process the greater is the tendency to the degeneration and softening of the nodules, the less intense and more chronic, the more liable are the miliary lesions to become fibroid.

LOCAL TUBERCULOSIS.—Before concluding the consideration of the general pathology of tuberculosis, allusion must be made to those cases in which the tuberculous processes are confined to a single organ. This limited tuberculosis differs from the more general one only in the extent of the distribution of the infective materials. The miliary lesions originate from some retrograde inflammatory product situated usually in the same organ as that in which they occur, and their limitation is probably owing to the infective substances being disseminated by the lymphatics and serous canals and not by the bloodvessels. This will be again referred to in the chapter on “Pulmonary Phthisis,” and also in the following description of the tuberculous process as it occurs in the several organs and tissues.

CONCLUSIONS.—Having thus described the histological characters of tuberculous lesions, it remains to consider the relation which subsists between these lesions and the products of non-tuberculous inflammations. The tuberculous lesions being inflammatory growths—the result of the injurious influence of infective particles upon the small areas of tissue with which they come into contact—why do they differ from the tissue changes which accompany the ordinary less intense forms of inflammation? The answer to this question is at present far from satisfactory.

It must be admitted that constitutional conditions influence considerably the occurrence and character of tuberculosis. Tuberculous processes occur, for the most part, in the scrofulous, and the products of some scrofulous inflammation are the most frequent infective agents. Constitutional conditions may probably thus so modify an inflammatory process as to give to its products infective properties. It must, I think, also be regarded as probable that conditions of the constitution may influence the effect produced by the dissemination of the infective particles, and that these particles, whether derived from a caseous or non-caseous focus, may in certain conditions of the constitution give rise to tuberculous processes, whilst in others their dissemination is unattended by change.

The histological peculiarities of the tuberculous lesions appear also to depend mainly upon constitutional conditions. The influence of scrofula upon the histological changes which accompany inflammation has already been seen, and from the close histological relationship

which subsists between the disseminated nodules met with in tuberculosis and the more diffused lesions produced by primary inflammation in scrofulous subjects, and also from the fact that it is in the scrofulous that tuberculosis most frequently occurs, we may, I think, assume that the characters of tuberculous lesions also are dependent upon a constitutional state.

In both scrofulous inflammation and tuberculosis there is a tendency to the development of large cell-forms and to the formation of a lowly organized and non-vascularized structure which soon undergoes retrograde changes. These characters of the inflammatory new growth appear to me to be probably due to the inflammatory process occurring in tissues of such low vitality that the cellular inflammatory products are incapable of forming an organized vascular tissue, but merely undergo some increase in size and then tend to slowly degenerate. The protoplasm grows, the nuclei multiply, but the higher manifestation of vitality—the subsequent division of the protoplasmic mass—does not take place, and thus are produced the giant cells.

Tuberculosis of the Pia Mater.

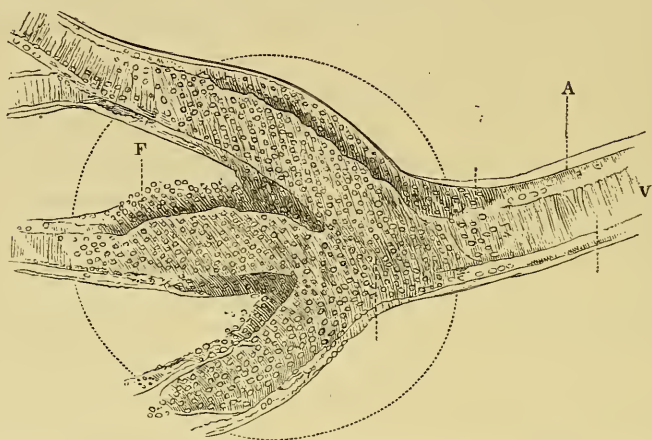
In the pia mater the tuberculous process is associated with inflammation of the meninges, constituting the condition known as *tubercular meningitis*. This is almost invariably a part of a general tuberculosis.

The process is almost exclusively confined to the pia mater as the base of the brain, and the tuberculous nodules—which may easily escape observation—are seen in connection with the small arteries in the Sylvian fissures, and deeply seated between the convolutions. A few scattered granulations are, however, frequently visible on the upper surface of the hemispheres. The inflammatory growth originates in the perivascular lymphatic sheaths which inclose the small arteries of the pia mater. (Fig. 82.) The cells of the sheath multiply, and the process of proliferation commencing at separate centres, numerous small gray nodules are produced around the vessel. These, which are distinctly visible to the naked eye, cause an external bulging of the sheath, and a diminution in the calibre, or even complete obliteration, of the inclosed vessel.

The localized obstructions to the circulation which result from the pressure of the perivascular nodules cause intense hyperæmia of the

collateral vessels, and thus the pia mater at the base of the brain becomes exceedingly vascular, there being in some cases rupture of

FIG 82.



Miliary Tubercle in the Pia Mater.—The dotted line indicates the original size of the tubercular nodule. A. The lymphatic sheath. V. The bloodvessel. F. Proliferation of elements within the sheath. $\times 100$. (Cornil and Ranvier.)

the vessels and extravasation. This is followed by a more general inflammatory process—a true basic meningitis. A transudation of the liquor sanguinis takes place from the hyperæmic and injured vessels, blood-corpuscles escape, and thus the meshes of the pia mater become infiltrated with a sero-fibrinous, and often purulent liquid.

The changes in the pia mater at the base of the brain are attended by softening of the immediately subjacent cerebral substance, which becomes infiltrated with young cells. The lateral ventricles at the same time become distended with serum (acute hydrocephalus), so that the convolutions on the surface of the hemispheres are seen to be much flattened. The ependyma and choroid plexus also become exceedingly vascular, and the walls of the ventricles, together with the fornix and soft commissure, become much softened. All of these changes are owing, partly to an inflammatory process, and partly to the mechanical obstruction to the circulation caused by the tuberculous growth. In addition, the arachnoid membrane is dry and sticky.

TUBERCULOUS MASSES IN THE BRAIN.—In addition to the miliary lesions occurring in the pia mater in tubercular meningitis, large tuberculous masses are occasionally met with in the brain unassociated with a general tuberculous process. These masses, which vary in size

from a hazelnut to a hen's egg, commonly occur in the cerebral substance, especially at the base of the brain. They are of a pale yellow color and firm consistence, and usually form quite round globular tumors. Their surface is often seen to be covered with minute gray nodules, which extend into the surrounding tissue; and on section, similar nodules are sometimes visible, scattered through the substance of the tumor. In most cases only one or two such masses are found, but occasionally they are more numerous. They occur especially in childhood, and usually in children in whom there is a general tendency to caseation of inflammatory products ("scrofulous" children). When examined microscopically they are found to be made up of an adenoid structure and large branched cells, such as has been already described as so characteristic of tuberculous lesions. This structure—which is best seen in the peripheral portions of the tumor—is often concentrically arranged around bloodvessels, and is found undergoing in different parts fibrous and caseous metamorphosis.

Respecting the nature of these masses and the way in which they originate, it is difficult to speak with certainty. From the fact that miliary nodules are so often to be seen on their surface and extending into the surrounding tissue, it is supposed that they originate by the aggregation of such nodules—that the primary nodule constitutes an infective focus, and so causes a succession of growths in its immediate vicinity. This hypothesis is probably correct. Occasionally the tuberculous mass causes a more general infection, and so gives rise to tubercular meningitis or to a general tuberculosis.

Tuberculosis of Lymphatic Glands.

In the lymphatic glands, tuberculous processes give rise, in the first place, to changes in the peripheral portions of the gland, inasmuch as it is with these that the infective materials which are conveyed by the lymphatic vessels first come into contact. The active changes in the gland begin with the formation of a large multinucleated branched cell. (Fig. 83.) In the earlier stage of the process small gray nod-

FIG. 83.



Tuberculosis of a Lymphatic Gland.—The earliest stage of the process, showing the giant cell. $\times 200$.

ules are visible scattered through the cortex. These gradually increase in size and become caseous. The gland then becomes enlarged, the distinction between its medullary and cortical portions becomes lost, and it becomes changed to a grayish homogeneous mass, in which are varying sized tracts of caseous materials. The new growth very frequently undergoes a marked fibroid development; so that the caseous masses are surrounded by a dense fibroid structure. The caseous portions of the gland may subsequently soften, dry up, or calcify.

Tuberculosis of Mucous Membranes.

In mucous membranes the development of tuberculous nodules is usually secondary to some primary inflammatory process which leads to ulceration of the membrane. The intestinal, the urino genital, and the respiratory mucous membranes may all be the seats of a tuberculous growth.

The Intestine.—In the intestine the occurrence of true tuberculous processes appears to be almost invariably preceded by primary inflammatory changes in the intestinal lymphatic structures. These changes have their seat in the solitary and Peyer's glands, and, as in typhoid fever, it is especially these structures in the lower part of the small intestine and in the cæcum which are affected.

The first stage of the process consists in an inflammatory hyperplasia of the lymphatic elements. In Peyer's patches this hyperplasia usually affects isolated follicles in the patch. The solitary glands and certain follicles in the patches thus become swollen, and project with undue prominence above the surface of the membrane. The newly formed elements then undergo retrogressive changes—they soften, the degeneration in the patches commencing at several separate centres, and often extending until the whole patch becomes destroyed. As the result of these primary inflammatory changes an ulcerated surface is produced, the floor and edges of which are more or less thickened, owing to the extension of the inflammatory infiltration into the sub-mucous connective-tissue. This is a simple ulcer, and its production, so far, is quite independent of a tuberculous process.

What must be regarded as a tuberculous change occurs subsequently to the primary ulceration, and it consists in the development of small nodules of new growth in the floor of the primary ulcer. The development of these nodules appears to take place principally around the bloodvessels, and as these are arranged transversely around the intes-

tine, the new growth proceeds in the same direction. These secondary nodules of new growth, like the primary inflammatory product, soften and become caseous, and thus the process of ulceration gradually extends transversely until the whole circumference of the gut may be destroyed.

The ulcer thus produced presents a strong contrast to that of typhoid. Its edges and base are thickened and indurated, and the tuberculous nodules, tending to become caseous, are seen scattered in its floor. (Fig. 84.)

The tubercular ulcer rarely, if ever, heals. Owing to the thickening of the tissues at its base, perforation is quite an exceptional occurrence. In the process of its extension the ulceration is attended by some contraction and narrowing of the gut.

Tuberculosis of the Lungs.

Tuberculous processes occur in the lungs as a part of a general tuberculosis, and also in many cases of pulmonary phthisis. The nature of the resulting inflammatory lesions is similar in both. It will be well however, in the present place, more particularly to describe these lesions as they occur in the general infective disease. The more limited processes which take place in phthisis will be again referred to in a subsequent chapter devoted to the consideration of this affection. (See "Pulmonary Phthisis.")

The pulmonary lesions met with in general tuberculosis consist, for the most part, of disseminated nodular growths, which are universally known as miliary tubercles. These growths are of two kinds—the *gray* and the *yellow*. The *gray* are semi-transparent nodules of a grayish-white color, varying in size from a small pin's head to a hemp seed. They are somewhat spherical in shape, but usually possess a well defined outline. Sometimes they are firm and almost cartilaginous in consistence; whilst in other cases they are much softer and almost gelatinous. The softer forms, instead of being semi-transparent, are more opaque and white. The *yellow* are, for the most part, larger than the preceding, many of them much so, some being as large as a pea. They are also softer in consistence, less defined and regular in outline, and they pass more insensibly into the surrounding tissue. Many of them possess a grayish-white translucent margin,

FIG. 84.



A Tubercular Ulcer of the Intestine.—(Diagrammatic.) *a.* Epithelial lining. *b.* Submucous tissue. *c.* Muscular coat. *d.* Peritoneum.

which may be pretty firm in consistence, but never so hard as are many of the gray nodules, whilst their central portions are opaque, yellowish, or caseous.

Both the gray and the yellow nodules are often found associated in the same lung; in other cases the gray nodules only are met with; whilst, less frequently, nearly all the growths are of the yellow variety. The condition of the pulmonary tissue which is situated between the nodules varies considerably. It may be perfectly normal, more or less congested and œdematous, or it may present varying sized tracts of grayish, granular, friable consolidation. A perfectly normal condition of the intervening pulmonary tissue is found in many of these cases in which all the growths are of the firm, gray variety; but when there are numerous yellow or soft gray nodules the lungs are nearly always more or less congested or consolidated.

When these nodules are examined microscopically they are seen to exhibit two different kinds of structure—viz., the adenoid structure with branched multinucleated cells, which has been already described as that which is the most characteristic of tuberculous lesions, and

FIG. 85.



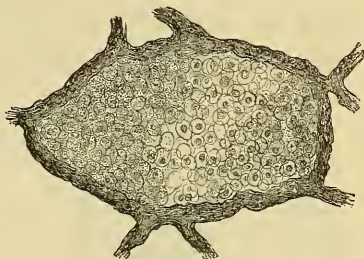
A small soft Gray Tubercle from the Lung in a Case of Acute Tuberculosis.—The whole of the tubercle is shown in the drawing, and it is obviously constituted largely of *intra-alveolar* products. $\times 100$, reduced to $\frac{1}{2}$.

accumulations of epithelial cells within the pulmonary alveoli (catarrhal pneumonia). There is, however, this marked difference between the various kinds of nodules—that whereas the smaller firm gray ones

are constituted almost entirely of the first named structure, the larger soft gray, and most of the yellow ones, consist largely of the intra-alveolar accumulations.

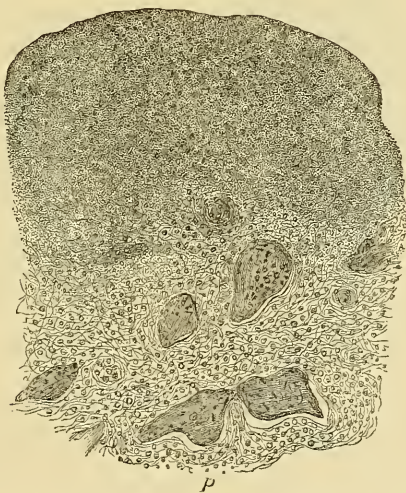
First, with regard to the soft gray and yellow nodules. Most of these when examined with a low magnifying power present the appearance represented in Fig. 85, the nodules evidently consisting largely of accumulations within the alveolar cavities. When more highly magnified their constitution becomes more apparent. It is then seen that the alveolar cavities are filled with epithelial elements and small cells resembling leucocytes, whilst the alveolar walls are more or less extensively infiltrated and thickened with lymphoid cells. (Fig. 86.) In many cases the central portions of the nodules will be seen to have undergone extensive degenerative changes, and to consist merely of a structureless

FIG. 86.



A portion of a small soft Gray Tubercle from the Lung.—This is from a case of acute tuberculosis, probably in an earlier stage than that from which Fig. 85 was drawn. The figure shows one of the alveoli filled with epithelial elements and a few small cells, with some cellular infiltration of the alveolar walls. $\times 200$.

FIG. 87.

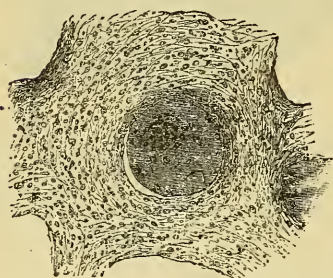


A portion of a Yellow Tubercle from the Lung in a Case of Acute Tuberculosis.—Showing the degeneration of the central portions of the nodule *c*, and the cellular thickening of the alveolar walls and accumulations within the alveolar cavities of the periphery *p*. $\times 100$.

granular debris, so that the accumulations within the alveoli and the cellular infiltration of the alveolar walls are only visible at their periphery. This is always the case in the distinctly yellow tubercles. (Fig. 87.)

The histological characters of the firmer gray nodules differ somewhat from the preceding. In these the cellular infiltration and thickening of the alveolar wall is much more marked, and many of the alveolar cavities are occupied by giant cells, these probably originating, as described by Dr. Klein, from the alveolar epithelium.¹ (Fig. 88.) In other cases, the alveolar structure has completely disappeared,

FIG. 88.



A portion of the more external part of a Gray Tubercle from the Lung in a Case of Acute Tuberculosis.—Showing the extensive infiltration and the thickening of the alveolar walls, and the giant cells within the alveolar cavities. × 100.

and the tubercle, when examined with a low magnifying power, appears as a little somewhat spheroidal mass, the cellular elements of which are seen to be grouped around separate centres. (Fig. 89.) When more highly magnified, these centres are seen to correspond with the large multinucleated branched cells already described, and the small-celled structure grouped around them, as is well shown in Fig. 79. This is a fully developed tubercle of the lung. The small-celled structure at the peripheral portions of the nodules extends

into and produces a thickening of the walls of the alveoli with which the nodule is incorporated. (Fig. 90.) In the tubercles thus constituted, extensive retrogressive changes rarely occur. Degeneration is slow and very incomplete, and the nodule often becomes imperfectly fibroid.

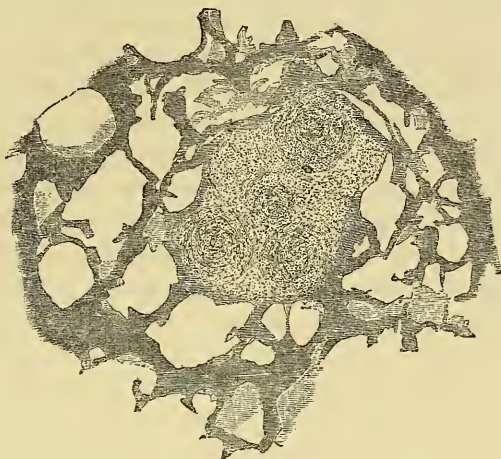
Respecting the cause of these differences in the histological characters of the miliary lesions in the lungs—I believe them to depend upon differences in the age of the nodules, and in the intensity of the tuberculous process.² If the intensity of the process be con-

¹ These large multinucleated cells are stated by Dr. Klein (*loc. cit.*) to originate either by the fusion of the alveolar epithelium, or by the excessive development of an epithelial cell. Since the publication of Dr. Klein's statement I have frequently observed these cells situated distinctly in the alveolar cavities, and I have little doubt they originate in the way he describes.

² Intensity comprises two factors—severity of injury and susceptibility of injured tissue. In scrofula, for example, the susceptibility of the tissue is great,

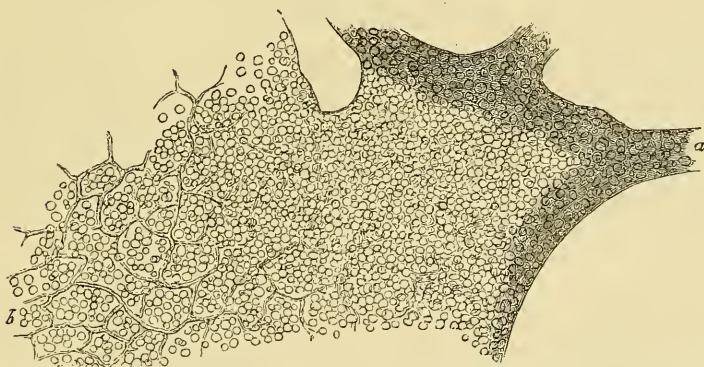
siderable, the nodules will consist in the main of accumulations of epithelium within the pulmonary alveoli, and the nodule will rapidly

FIG. 89.



A firm Gray Tubercle from the Lung in a Case of Acute Tuberculosis.—Showing the grouping of the elements around separate centres, the nodule consisting of several giant-cell systems.
 X 33.

FIG. 90.



A small portion of the most external part of a firm Gray Tubercle from the Lung in a Case of Acute Tuberculosis.—Showing the incorporation of the nodule with the alveolar wall a.
 X 279.

undergo disintegration. (See Fig. 87.) If the process be less intense, and the nodules attain a more advanced age, degeneration will be less rapid and complete, the cellular infiltration and thickening

and the intensity of tuberculous processes is often considerable. (See "Inflammation.")

of the alveolar walls will be greater, and the epithelial elements may form large multinucleated cells. (See Fig. 88.) Lastly, in the least intense and most chronic processes, the development of multinucleated elements and the formation of the network of branched cells reaches its maximum (see Figs. 79 and 89), degeneration takes place slowly in the central portions of the nodule, and there is often considerable fibroid induration of the new tissue. There is thus a close analogy between the tissue changes resulting from tuberculosis of the lungs and those which result from other inflammatory processes. (See "Chronic Inflammations.") The degeneration of the lesions is mainly owing to the interference with their vascular supply, caused by the pressure exercised upon the bloodvessels by the intra-alveolar accumulations, and the obliteration of the vessels by the cellular infiltration of the alveolar walls.¹

CHAPTER XXXII.

PYÆMIA AND SEPTICÆMIA.

THE diseases known as Pyæmia and Septicæmia result from the absorption and dissemination of septic substances, derived usually from the products of some acute inflammation. They are very closely allied, and very frequently associated. Septicæmia, however, is a somewhat more simple process, and it will therefore be considered first.²

Septicæmia.

By Septicæmia is generally understood those forms of septic poisoning which are unaccompanied by the development of secondary centres of inflammation or suppuration.

¹ For a more complete account of Pulmonary Tuberculosis see "The Pathology of Pulmonary Consumption." By the Author, 1878.

² The terms pyæmia and septicæmia are used in different senses by different pathologists, and our knowledge of these and allied processes is still undoubtedly incomplete. The report of the Committee appointed by the Pathological Society of London to investigate the nature and causes of Pyæmia, Septicæmia, and Purulent Infection, is an admirable account of what is at present known of these subjects. *Trans. Path. Soc. Lond.*, 1879.

When a person receives an external injury sufficient to produce a wound of considerable extent, the resulting inflammatory process is usually followed by a general disorder of the vital functions, the most prominent symptom of which is pyrexia. This pyrexial state, which so commonly occurs after surgical operations and other extensive local injuries, is what is usually known as *traumatic* or *surgical fever*. Respecting the cause of this fever—it is probably mainly due to the absorption of small quantities of decomposing matter from the surface of the wound. Whatever, therefore, prevents septic changes in the inflammatory products, or interferes with the absorption of the septic fluids, will prevent the fever. Absorption, as will be seen presently, is prevented by the formation of healthy granulation tissue.

Closely allied to this traumatic or surgical fever is the condition known as *septicæmia*. Here, also, there is an absorption of septic matter from some local lesion, but the general disturbance of the vital functions to which it gives rise is much more considerable. Septicæmia appears therefore to differ from simple traumatic fever mainly in this—that in it the infective process is one of much greater intensity. No sharp line of demarcation, however, can be drawn between the two.

The clinical phenomena of septicæmia, as observed in man, are characterized not only by pyrexia, but also, in severe cases, by vomiting, diarrhœa, muscular enfeeblement, affecting particularly the heart and respiratory muscles, and ultimately a condition of collapse which tends to terminate in death. After death the blood is found to be darker and less firmly coagulated than usual. Extreme congestions and ecchymoses are met with in internal organs, especially in the heart, lungs, and gastro-intestinal mucous membrane. The spleen, liver, and other viscera are enlarged, friable, and abnormally vascular; and little patches of lymph are seen on the pleura and pericardium. Metastatic abscesses and all other secondary inflammatory lesions are completely absent. Such pure uncomplicated cases of septicæmia are, however, comparatively infrequent, the septicæmia being usually associated with the development of secondary inflammations—a pyæmia. A simple septicæmia is perhaps most common in the puerperal state (Puerperal Septicæmia).

In studying the pathology of septicæmia we must consider—1. The nature of the infective material—the septic poison, and the conditions under which it is produced; 2. The circumstances which influence its absorption and dissemination; and 3. The changes which

it produces in the circulating blood. Our knowledge on all these questions has been derived mainly from the experimental investigation of infective processes induced in the lower animals; and amongst those who have contributed most largely to this knowledge during the past few years are Professors Billroth, Bergmann, Koch, and in our own country, Dr. Burdon Sanderson.¹

1. *The Septic Poison*.—First, with regard to the infective material, and the circumstances under which it is produced. In the natural disease this material originates in connection with some local inflammation, or much less frequently with some wound in which no inflammation is present—as the uterus after delivery. It is in the albuminous liquids of such local lesions that the septic poison is produced, and its production appears to be invariably associated with the *putrid decomposition* of the liquid. In the disease artificially induced in the lower animals the poison is introduced from without, and consists of some putrid liquid, such as a putrid infusion of muscle.

It is well known that the putrid decomposition of albuminous

liquids is always associated with the presence in them of *bacteria*, or their germs. (Fig. 91.) In a series of experiments made in the laboratory of the Brown Institution in 1872, with the object of determining the nature of the septic poison, Dr. Sanderson found that these, or similar organisms, abounded in all liquids which were capable, when introduced into the circulation of an animal, of producing septicæmia;² and from the results of



Fetid Pus from an Empyema.—Showing common forms of bacteria amongst the pus-corpuscles. $\times 600$.

these and other more recent experiments, Dr. Sanderson concludes that *the agency of bacteria is essential for the production of the septic poison*.

But although the production of the poison appears to be invariably associated with the presence of bacteria, it is something quite distinct from the process of simple putrefactive decomposition. That this is so has been proved by Bergmann, who has shown that the poison can be produced by the action of bacteria on non-albuminous liquids; and also that if bacteria be grown in such non-albuminous liquids, the

¹ "Lectures on the Infective Processes of Disease," by Dr. Burdon Sanderson, delivered at the University of London: *Brit. Med. Journ.*, Dec. 1877, and Jan. 1878.

² "Trans. Path. Soc. Lond.," vol. xxiii. 1872.

first crop, which are rod-shaped, active organisms (bacteria proper) are inert; but as the process of cultivation proceeds, spheroidal and less active organisms are produced (micrococci), and the liquid becomes intensely virulent. From these facts Dr. Sanderson infers that the poison is not a product of the septic disintegration of protein substances, but something much more intimately associated with the existence and growth of the organisms themselves.

The production of the poison being thus dependent upon the agency of bacteria, the question arises whether its effects are due to the direct action of the organisms themselves. In answer to this question, the results of Dr. Ander's experiments appear to be conclusive. This observer has shown that the complete destruction of the organisms in a liquid which has been proved to be septic in no way impairs the virulence of its action.¹

From these investigations we must therefore conclude that the septic poison is a product of the growth of bacteria; but, says Dr. Sanderson, *bacteria are incapable of producing the poison in the healthy organism*. The condition which appears to be necessary for the development of the poison, is some abnormal state of the living tissues, such as is produced by injury. It is in the products of such injured tissues that the development of the bacteria and the production of the poison can take place, and it is consequently in some inflammatory lesion that septic processes most frequently originate.

Inasmuch as the agency of bacteria is essential for the production of the septic poison, it will be readily understood why, in the majority of cases, septicæmia originates from lesions which are in direct communication with the *external air*, and also why the development of septic processes is favored by the crowding together of persons with open wounds; for, as pointed out by Mr. Savory, the decomposition of an animal fluid is hastened by the introduction into it of any other animal matter which is also undergoing active putrefactive change.²

2. *The absorption of the Poison*.—Having discussed the nature of the poison, and the circumstances under which it originates, it remains to consider how it becomes absorbed and disseminated. Putrid liquids in contact with injured tissues—liquids capable of producing the most intense septic processes if artificially inoculated—do not always

¹ Ander's "Giftige Wirkung von durch Bakterien betrückte Nahrflüssigkeit:" *Deutsche Zeitschrift für Chirurgie*, vol. vii.

² "Discussion on Pyæmia at Clinical Society." Mr. Savory.—*Trans. Clin. Soc. Lond.*, vol. vii. p. lxxvi.

become absorbed. The causes which in some cases favor their absorption, and in others prevent it, must be looked for, according to Mr. Savory (*loc. cit.*), in the condition of the tissues with which they are in contact. A fresh wound is a very readily absorbing surface, but Billroth and others have shown, experimentally, that healthy granulations offer a decided obstacle to the absorption of fluids from their surface. When, however, the granulations become partially destroyed, or are in an unhealthy condition, fluids readily permeate them. It must, then, be considered as exceedingly probable that the absorption of the poison is intimately connected with some abnormal condition, due to injury or disease, of the tissues with which it is in contact. The poison, when absorbed, is disseminated by means of the veins and lymphatics.

3. *Changes produced by the Poison in the Blood.*—Respecting the changes produced by the septic poison in the circulating blood, and in the organism generally—the results of the experimental production of septicæmia show that, in many cases, these are in direct proportion to the quantity of the poison that is introduced; whilst in others the poison *multiplies* after its absorption, and its effects, therefore, are not proportionate to the quantity absorbed, but the intensity of the process gradually increases. In the former case the blood, merely containing the original quantity of the poison much diluted, is incapable of setting up a similar process in another animal; whereas in the latter, inasmuch as the poison increases, the smallest drop of blood may be intensely infective. Clinically, these two classes of cases are still very imperfectly distinguished.¹ The multiplication of the poison will be again alluded to when speaking of pyæmia.

Before concluding this part of the subject, further allusion must be made to the character of the blood in septicæmia, and to the changes which are observed in the organs after death. The extent to which the blood is altered varies considerably, both in septicæmia and pyæmia, according to the virulence of the poison. In the more severe

¹ According to the report of the committee appointed by the Pathological Society, already alluded to, those cases of septicæmia in which there is no multiplication of the poison in the blood are due simply to the absorption of the chemical products of putrefaction ("Septic Intoxication"); those cases in which the poison multiplies and in which the disease is truly infective (communicable by inoculation from animal to animal) depend upon the absorption of some virus which is developed in the decomposing organic matter ("Septic Infection"). The two conditions may be associated.—*Trans. Path. Soc. Lond.*, 1879.

cases this fluid is darker in color and coagulates less perfectly than in health. The red corpuscles also tend to aggregate in clumps instead of rouleaux; and they often undergo disintegration during life, so that the serum is stained with hæmoglobin immediately after death.

One of the most important features, however, in connection with the blood is the marked tendency to congestion and blood stasis which characterizes both the natural and the artificially induced diseases. With regard to the causes of these circulatory phenomena—the investigations of Dr. Köhler appear to show that they are partly due to the destructive action of the poison on the white blood-corpuscles, and the consequent liberation of the ferment upon which process of coagulation depends.¹ (See “Thrombosis.”) From the report of the committee appointed by the Pathological Society, three other circumstances appear to be concerned in their production—viz., the occlusion of the small bloodvessels by micrococci, the destruction and shedding of the vascular endothelium, and hypertrophy of the intima. The microscopical examination of the various organs from cases of septicæmia and pyæmia by the members of this committee showed that the capillaries were frequently occluded by dense aggregations of minute spherical organisms imbedded in a homogeneous substance; and that similar organisms adhered in masses to the walls of the larger vessels. Bacteria were found much less frequently. The endothelium of the bloodvessels generally was here and there detached; and the intima was often considerably thickened, in some cases so much so as to considerably diminish the lumen of the vessel. The importance of these changes as causes of congestion and thrombosis is sufficiently obvious.

Pyæmia.

Pyæmia, as already stated, appears to result from the development and absorption of the same poison as that which gives rise to septicæmia. The two conditions are thus closely allied, and they are very often associated.

Pyæmia differs from septicæmia in this respect—that in it the absorption and dissemination of the poison gives rise not only to an alteration in the blood and a general disturbance of the vital functions,

¹ “Ueber Thrombose und Transfusion, Eiter und septisch Infection und deren Beziehung zum Fibrinferment,” by Dr. Armin Köhler. Dorpat, 1877.

but also to the production of secondary foci of inflammation—the so-called *metastatic abscesses*. It is the production of these abscesses, and of other more diffused inflammatory lesions, which is the distinctive character of pyæmia. It is thus probable that pyæmia is invariably associated with more or less septicæmia, and it may be regarded as a septicæmia in which there are disseminated inflammations and suppurations.

Pyæmia being thus the result of the absorption of the same poison as that which gives rise to septicæmia, all that has been said respecting the origin and nature of this poison, and the circumstances which influence its absorption and dissemination from the focus of infection, applies equally to both diseases. What remains for consideration are the differences in the effects which are produced. It will be well, in the first place, however, to describe briefly the pyæmic lesions.

The lesions which are the most characteristic of pyæmia are the so-called metastatic abscesses. These present certain peculiarities. In their earlier stages they usually consist of somewhat reddish, friable, granular-looking masses of consolidation, which are surrounded by a thin zone of red hyperæmic tissue. These masses are frequently wedge-shaped, the apex of the cone being towards the centre of the organ. They vary considerably in size, some not being larger than a small pea, whilst others exceed the size of a chestnut. The consolidated mass soon assumes the characters of an abscess. Its more central portions become softened and purulent, and ultimately it tends to become converted into a collection of pus and broken-down tissue, this being still surrounded by a thin red zone of induration. These metastatic abscesses are met with most frequently in the lungs; but they also occur in the liver, spleen, kidneys, and in other internal organs. They are more commonly found near the surface than in the more internal portions of the organ, often being situated immediately beneath the fibrous capsule.

In addition to these abscesses, more diffused inflammatory lesions are met with in pyæmia. These consist chiefly of suppurative arthritis, and of inflammations of the subcutaneous cellular tissue and serous membranes, especially of the pleuræ and pericardium.

With regard to the pathology of the metastatic abscesses—they are, for the most part, of *embolic* origin, the emboli originating in the thrombi which form at the seat of the primary lesion. The circumstances under which thrombi formed in the vessels of a part become softened or broken-up, so as to furnish embolic plugs, and the way in

which these plugs may set up acute inflammatory processes at the seat of their arrest, has been described in the chapters on "Thrombosis" and "Embolism." It will be sufficient in the present place to state that in the course of a pyæmic process the coagula which form in the vessels at the seat of the pyæmic inflammations become infected with the pyæmic poison, and if they soften or become broken up so as to furnish embolic plugs, these plugs cause secondary suppurative processes in the parts in which they become arrested; and it is to the dissemination of these infective emboli that the formation of the majority of the metastatic abscesses in pyæmia is owing. The more diffuse secondary inflammations of the subcutaneous connective tissue, and of serous and synovial membranes, are probably often unconnected with embolism, but are due directly to the altered condition of the blood.

The prominent part which is played by thrombosis and embolism in the pathology of these infective processes probably accounts for the fact, that these processes are, in the majority of cases, associated with the development of metastatic abscess and other secondary inflammations—in other words, that pyæmia is so much more common than pure septicæmia. The bloodvessels of the primary lesion which serves as the starting-point of the infective process—usually a local inflammation—can rarely be free from coagula, and hence not only is the absorption of the poison often delayed (or even prevented), but, when it does take place, it is usually associated with the dissemination of solid substances derived from the coagula themselves (emboli).

The occurrence of thrombosis and embolism also appears, in some cases, to influence the intensity of the infective processes. In simple septicæmia it has been seen that the changes produced are often in direct proportion to the quantity of the poison which is absorbed from the primary lesion. In pyæmia, however, Dr. Sanderson says, the poison probably multiplies within the organism. In attempting to explain this, the experiments on the cultivation of the poison are of much value. These experiments prove not only that the poison can be produced by cultivation, but also that in an artificially produced septic liquid the virulence of the liquid increases with the development of the bacteria. A similar cultivation of the poison probably sometimes occurs in pyæmic processes, the original poison produced at the primary lesion increasing in the secondary and tertiary foci of inflammation, and not only increasing, but perhaps becoming more virulent.

Although, however, this may occur in some cases of pyæmia, it is by no means constant. In many cases secondary inflammations are the principal result of the dissemination of the septic emboli, and there is but little general blood poisoning.

CHAPTER XXXIII.

SYPHILIS.

THE lesions occurring in the course of constitutional syphilis are for the most part inflammatory in their nature, but in their seat, distribution, and histological characters, many of them present certain peculiarities which make them quite characteristic of this disease. The primary syphilitic lesion (usually the indurated chancre), the secondary lymphatic gland enlargement, and the subsequent series of changes in the skin, mucous membranes, and later—in the nervous system, bones, and internal organs, are all of them the results of chronic processes, allied to inflammation, induced by the syphilitic poison.

The lesions, however, which must be regarded as especially characteristic of syphilis, are of three kinds—certain fibroid indurations, a form of growth which is known as a *gumma* or syphilitic tumor, and certain changes in the arteries. These forms of lesions are very frequently associated, and in many cases it is difficult to draw any line of demarcation between them.

1. *Fibroid Changes*.—Fibroid indurations are often associated with the gummata, and many fibroid lesions are simply the remains of what were previously gummy tumors.

Fibroid changes also occur very frequently in the course of syphilis quite independently of gummata. These changes consist in the development of a fibroid tissue precisely similar to that met with as the result of ordinary chronic inflammation. (See “Inflammation of Common Connective Tissue.”) The new tissue, which originates around the bloodvessels, and in the earlier stages of its growth is more or less richly cellular, produces a fibroid thickening of the affected area. These fibroid thickenings are characterized by their

localization and by the irregularity in their distribution. They occupy, for the most part, *small areas*, and the *surrounding tissues are unaffected*. It is these peculiarities in their distribution and localization, and not their histological characters which render them so characteristic of syphilis.

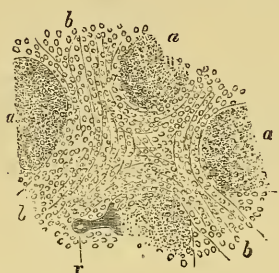
These fibroid changes are met with in various situations—in the periosteum, in the sheaths of nerve-trunks, in the capsules and interstitial tissue of organs, and in muscle. When occurring in the capsules of organs they present very characteristic appearances. In the liver and spleen, where they are the most frequent, they give rise to irregularly disturbed thickening and puckering of the capsule, which is exceedingly typical of advanced syphilis. The thickened portions are usually connected with dense fibroid septa which pass into the interior of the organ; and there are frequently also numerous strong peritoneal adhesions. The gummy masses, about to be described, are very often to be found in the midst of the fibroid growth.

2. *Gummata*.—These are perhaps more characteristic of syphilis than the fibroid lesions, with which, as already stated, they are frequently associated. The gummata, as usually met with, are moderately firm yellowish-white nodules, having often, on section, somewhat the appearance of a horse-chestnut. They vary in size from a hemp-seed to a walnut, and are surrounded by a zone of translucent fibrous-looking tissue, which sometimes has the appearance of a capsule, and which is so intimately associated with the surrounding structures that the enucleation of the mass is impossible. In the earlier stages of their development, when they less commonly come under observation, they are much softer in consistence, more vascular, and of a reddish-white color; whilst in their more advanced stages, owing to extensive retrogressive changes, they may be distinctly caseous.

When the gummata are examined microscopically they are found to consist in the main of atrophied, degenerated, and broken-down cell-products, embedded in an incompletely fibrillated tissue. There are, however, some marked structural differences between the central and external portions of the growth. The central portions are composed almost entirely of closely packed granular débris, fat granules, and cholesterin, amongst which may be an exceedingly scanty fibrillated tissue. (Fig. 92 *a*.) Surrounding this and directly continuous with it is a fibro-nucleated structure; whilst the peripheral portion of the growth is a richly cellular and vascular tissue. (Fig. 92 *b*, and Fig. 93.) This peripheral cellular tissue, which is in direct histological con-

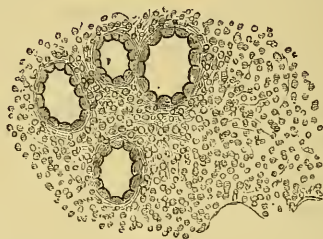
tinuity with the surrounding structures, consists of small cells, many of which resemble white blood-corpuscles, whilst others are larger and nucleated like the cells of granulation-tissue. These cells are separated by a scanty, homogeneous, intercellular material and numerous new bloodvessels.

FIG. 92.



Gummy Growth from Liver.—*a.* Central portions of growth consisting of granular debris. *b.* Peripheral granulation tissue. *r.* A bloodvessel. $\times 100$. (Cornil and Ranvier.)

FIG. 93.



The Peripheral Portion of a Gummy Growth in the Kidney.—Showing the small-celled granulation growth in the intertubular tissue. $\times 200$.

The three zones already described, which are to be distinguished more or less clearly in most of the fully developed gummy nodules, correspond with three different stages in their growth. The most

FIG. 94.



From a Gummy Growth in the Kidney.—Showing the reticulated structure occasionally met with in the intermediate zone of these formations. $\times 200$.

external zone, consisting of the vascular granulation-tissue, represents the earlier stage of development, and by the continuous formation of this tissue the growth may continuously increase. The intermediate more fibrous zone represents the second stage in the process—the development of the granulation-tissue into a more or less completely fibrillated structure. The characters of this fibrillated tissue vary in different growths. In some the fibrillation is very distinct; in others, the tissue is dense and cicatricial in character; whilst, less frequently, it consists of a reticulated structure within the meshes of which are grouped round small cells.

(Fig. 94.) The central zone, consisting of the amorphous granular

material, represents the oldest portion of the growth—that which has undergone retrogressive changes. The bloodvessels, which only exist in the zone of proliferation, appear to become obliterated in the process of development, and this accounts for the rapid degeneration of the central portions of the growth. It is probable that this obliteration of the bloodvessels may be due to the changes in the arteries about to be described. When the tumor is large, it may sometimes be seen to be made up of several distinct smaller growths, each presenting at its circumference the more perfect cells, whilst its central parts are granular and amorphous.

It would thus appear that the first stage in the process of formation of these gummy growths consists in the production of a highly organized and vascular granulation-tissue. This new tissue, although it may develop into an incompletely fibrillated structure, soon undergoes degeneration. The degenerated elements become closely packed in the centre of the growth, whilst proliferation and incomplete fibrillation continue at the circumference. The central portions of the growth occasionally become calcified, but more commonly they gradually become absorbed, and a mere puckered fibrous cicatrix may thus ultimately occupy the seat of the original tumor. This is one of the ways in which the fibroid lesions originate.

The gummata are the new formations most characteristic of syphilis. They are met with in the skin and subcutaneous cellular tissue, in the submucous tissue, in muscle, fasciæ, bone, and in the connective tissue of organs—especially of the liver, brain, testicle, and kidney. They also occur, but much less frequently, in the lungs; as do also simple localized fibroid indurations. When situated in the submucous tissue, the mucous membrane usually becomes destroyed, and a deep ulcer forms. This is seen in the pharynx, soft palate, tongue, larynx, and in other parts. These true gummy ulcerations must be distinguished from the superficial ulcerations resulting from inflammatory processes in the lymphatic structures, which also occur in syphilis.

3. *Changes in Arteries.*—Certain changes in the cerebral arteries have been described by Heubner as characteristic of syphilis. These changes have been brought prominently before English pathologists by Drs. Greenfield, Barlow, and others;¹ and the investigations of the first named of these observers would tend to render it probable that similar changes occur in the arteries in other situations.

¹“Trans. Path. Soc. Lond.,” vol. xxviii.—*Visceral Syphilis*.

In the cerebral arteries the changes produce opacity and marked thickening of the vessel, with considerable diminution in its calibre. It is this diminution of the lumen of the vessel which is especially characteristic.

When transverse sections of the vessels are examined microscopically, the principal change is seen to be situated in the *inner coat*. It is well shown in the accompanying drawings made from specimens kindly lent to me by Dr. Barlow. (Fig. 95.) This coat is consider-

FIG. 95.



Syphilitic Disease of Cerebral Arteries.

A. Segment of middle cerebral artery, transverse section—*i*, thickened inner coat; *e*, endothelium; *f*, membrana fenestrata; *m*, muscular coat; *a*, adventitia. $\times 200$, reduced $\frac{1}{2}$.

B. Small artery of Pia Mater, transverse section.—Showing thickened inner coat, diminished lumen of vessel, and considerable infiltration of adventitia. The cavity of the vessel is occupied by a clot (? thrombus). $\times 100$, reduced $\frac{1}{2}$.

ably thickened by a cellular growth. The growth which is limited internally by the endothelium of the vessel (Fig. 95A, *e*), and externally by the membrana fenestrata (Fig. 95A, *f*), closely resembles ordinary granulation-tissue, consisting of numerous small round and spindle-shaped cells. This tissue appears gradually to undergo partial development into an imperfectly fibrillated structure.

In addition to this change in the intima, the outer coat is abnormally vascular and infiltrated with small cells (Fig. 95A, *a*), and this cellular infiltration usually also invades the muscular layer (Fig. 95A, *m*).

The result of these changes in the inner coat is to diminish very

considerably the lumen of the vessel (Fig. 95B); and the consequent interference with the circulation frequently leads to coagulation of the blood (thrombosis) and cerebral softening.

Dr. Greenfield's observations, as already stated, tend to show that similar arterial changes occur in other parts, and that they account for the degeneration of syphilitic gummata.

Syphilitic Disease of the Liver.

The liver is one of the most frequent seats of syphilitic lesions. The most common change is the development of fibroid and gummy growths in the substance of the organ. These growths are strictly localized, the surrounding liver-tissue being healthy. The growths—which are usually connected with fibroid thickenings of the capsule—sometimes consist simply of a dense fibroid structure. More commonly, however, gummy masses are found imbedded in the fibroid growth. In the former case it is possible that the gummy mass may have become absorbed, leaving merely its fibroid cicatrix.

The development of these growths produces very marked alterations in the form of the liver. Scar-like depressions are seen on its surface, and the organ is irregularly, and often very deeply puckered.

A more general fibroid change, not associated with the formation of gummy masses, is occasionally met with in the liver in inherited syphilis. This change closely resembles ordinary cirrhosis, although the intercellular network of the liver is usually more extensively involved.

Lastly, it must be mentioned that the liver in syphilis is frequently lardaceous.

It is unnecessary to describe particularly syphilitic lesions in other organs, as they all present the same general characters—viz., strictly localized fibroid, or fibroid and gummy growths.

CHAPTER XXXIV.

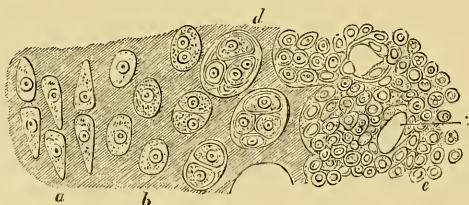
INFLAMMATION OF NON-VASCULAR TISSUES.

Inflammation of Cartilage.

THE phenomena of acute inflammation in cartilage, although comparatively rare in man, have been studied by the artificial production of inflammation in the articular cartilages of the lower animals. They consist in changes in the cartilage itself, and in the vessels of the adjacent synovial membrane and bone, from which the cartilage receives its nutritive supply. Respecting the vascular changes, these are such as have been already described as characteristic of inflammation.

The changes which take place in the cartilage itself have been believed to be accompanied by activity of the cartilage cells, by their proliferation, and the production of new elements. Such changes are represented in Fig. 96. The results of recent investigations, however, tend to show that the cells of the cartilage really remain inactive in the process of inflammation, and that all the young elements are emigrants from the vessels.

FIG. 96.



Section of Inflamed Cartilage.—*a.* The normal cartilage-cells. *b.* The same enlarged. *d.* Multiplication of cells within their capsules. *e.* Great increase in the number of the young cells, and destruction of the intercellular substance. $\times 250$. (Cornil and Ranvier.)

Whether the cells of the cartilage take any active part in the process or not, their capsules become destroyed, the intercellular substance softens and breaks down, and numerous small cells take the place of the original tissue. (Fig. 96 *e.*) As the process proceeds

the new cells and granular débris escape from the surface of the cartilage, which thus becomes irregular, presenting numerous elevations and depressions: this is acute ulceration of cartilage. Whilst these changes are taking place in the cartilage itself, numerous new blood-vessels are formed from those in the adjacent bone or synovial membrane; the little loops of new vessels dipping into the softened cartilage. This process of softening and ulceration may go on until the cartilage is completely destroyed, or it may become arrested. In the latter case the young cells form a granulation-tissue, this tissue fibrillates, and the lost cartilage thus becomes replaced by a fibroid structure.

When the inflammation is less severe and runs a more chronic course, the cellular infiltration is less abundant, and the intercellular substance is less destroyed. The newly formed cells are more highly organized, and whilst many of them undergo retrogressive changes, others form a fibrillated tissue. Irregular cavities may thus be produced in the midst of a fibrillated cartilage.

Erosion of Cartilage.—Allusion must be made here to a morbid condition of cartilage which is common in people past middle life. It consists in the occurrence upon the surface of the articular cartilages of small, yellowish, flocculent spots, which gradually increase in size, and ultimately break down and become destroyed, leaving a superficial erosion. The change occurs most frequently in the cartilages of the patella and of the knee-joint, and in other situations in which the cartilages are especially subjected to pressure.

When the diseased portions are examined microscopically, the most marked alteration is seen to consist in a fibrillation of the intercellular substance of the cartilage. Some of the cartilage-cells are also increased in size and show signs of proliferation; whilst others are in various stages of fatty metamorphosis. The change appears to result from long-continued irritation due to pressure, and it may be regarded as an irritative process, in which, owing to the natural poverty of the vascular supply, retrogressive changes occupy a prominent place.

Inflammation of the Cornea.

The process of inflammation as it occurs in the cornea has been chiefly studied in the frog. After injury of the frog's cornea, the earliest changes observed consist in the conjunctival epithelium becoming visible, and in the appearance amongst the epithelial cells

of a few leucocytes, which have probably escaped from the hyperæmic vessels of the conjunctiva. The cornea cells and their prolongations then become visible (they are invisible in the healthy cornea, which appears perfectly structureless), and the intercellular substance gradually becomes increasingly opaque, owing to its infiltration with small cellular elements (leucocytes). These are so numerous and increase so rapidly, that they must undoubtedly be regarded as, in the main, emigrant white blood-corpuscles. It was formerly believed that the cells of the cornea exhibited active changes, and that from them many of the new elements which are seen in the intercellular substance were produced; but here, as in cartilage, all recent investigations render it more probable that they really remain inactive. As the number of young elements increases the consistence of the cornea becomes diminished, until ultimately the tissue breaks down and is destroyed.

The inflammatory process may continue until the whole of the substance of the cornea is softened and destroyed; or it may become arrested. In the latter case more or less thickening and opacity of the cornea will result, owing to the increase in the number of cells and the changes in the intercellular substance.

CHAPTER XXXV.

INFLAMMATION OF COMMON CONNECTIVE TISSUE.

COMMON connective tissue is one of the most frequent seats of the inflammatory process, not only the subcutaneous connective tissue, but also the connective tissue of organs and of other parts.

If connective tissue be examined a few hours after the infliction of an injury, it will be found that in place of the fibrillated substance and fixed connective-tissue cells of which it is normally composed, the tissue is infiltrated with small round cells (leucocytes), and that the fibrillated intercellular material has become homogeneous and gelatinous in consistence. The number of these cells gradually increases, and the intercellular substance gradually becomes more completely destroyed, so that ultimately the tissue consists almost entirely of

small round cells, held together by a small quantity of soft gelatinous intercellular material.

Respecting the source from which these young elements are derived—*i. e.*, how far they are emigrants, and how far they are the offspring of cells belonging to the connective tissue—there appears to be little doubt that they are almost entirely emigrants; and it is also extremely probable that the escaped corpuscles multiply by division. It was formerly supposed that the connective-tissue corpuscles multiplied very rapidly in inflammation, and that the newly formed cells were entirely the result of their proliferation, but the investigations of Professors Cohnheim, Stricker, and others, show that this view is erroneous; and according to Cohnheim, these corpuscles take no part whatever in the inflammatory process. Professor Stricker, however, has observed them undergoing active movements in the inflamed tongue of the frog, and although he has never seen them divide, he concludes that they may probably do so in the latter stages of the inflammatory process. The present state of our knowledge respecting inflammation of connective tissue would therefore appear to justify the conclusion that in the early stages of the process all the young cells are emigrants, but that in the latter stages a few of them may possibly be derived from the proliferation of the fixed connective-tissue cells.

Such being the nature of the changes which more immediately follow injury of the connective tissue—the inflammatory process may terminate in *resolution*, in *organization*, or in *suppuration*.

RESOLUTION.—If the injury sustained by the tissue is not severe, the inflammation may gradually subside, the process terminating in *resolution*. In this case the hyperæmia diminishes, the emigration ceases, some of the young cells undergo fatty metamorphosis, others pass into and are removed by the lymphatics, and the tissue gradually returns to its normal condition. (See “Terminations of Inflammation.”)

ORGANIZATION.—If the inflammatory process does not terminate in resolution, many of the young cells may become more fully developed, and ultimately form a fibrillated tissue. This *organization* of the inflammatory formation or “productive” inflammation, is seen in the healing of wounds, the repair of ulcers, and also in many of the chronic inflammations of the kidney, liver, and other organs. In order for it to occur it is necessary that there should be a consider-

able diminution in the intensity of the inflammation. (See "Terminations of Inflammation.")

The process of organization consists in the development of many of the small round cells into larger elements, the formation of new blood-vessels, the fibrillation of the new structure, and its conversion into a mature connective tissue. These changes are similar to those which occur physiologically in the development of connective tissue from the cells of the embryo.

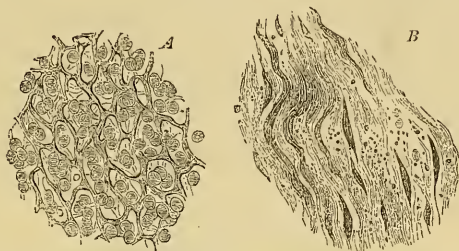
The first change observable in the small round-celled inflammatory production, usually about the fifth day, is the appearance in it of some larger elements. These are spherical masses of protoplasm, double the size of the smaller cells, with large round or roundly-oval nuclei, and slightly amœboid. The number of these larger cells increases, and some of them become more fully developed and contain two nuclei. Many of them also throw out processes and become branched, and the branches uniting with those of neighboring cells a more or less reticulated structure is produced, within the meshes of which are contained many of the smaller undeveloped elements (leucocytes). Somewhat later a few much larger masses of protoplasm containing several nuclei (myeloid cells) are seen, which help to form the branched reticulum. This structure, consisting, in the main, of single nucleated more or less branched cells, with often a few myeloid elements, constitutes what is known as *granulation-tissue*. With regard to the mode of development of this tissue from the primary inflammatory formation—it probably takes place, for the most part, by the progressive growth of some of the small cells, although the investigations of Zeigler seem to show that some of the larger may be formed by the union of some of the smaller elements.

Whilst these cell changes are taking place the tissue becomes permeated with new bloodvessels. These, which usually appear about the fourth or fifth day, are essential to development. If the tissue is incompletely vascularized it undergoes retrogressive changes. (See "Scrofulous Inflammation.") Our knowledge of the process of vascularization is still somewhat incomplete, but it is probable that the new vessels are formed by the canalization of the branched cells.

The next stage in the process consists in the development of the vascularized granulation-tissue into a fibroid or adenoid structure. Many of the small round cells now disappear, there is a tendency in the large ones to become lengthened and to assume a spindle shape, the bodies of the cells split up so as to form fibrils, the newly formed

capillaries gradually disappear, and the richly-cellular tissue thus becomes converted into a more or less dense structure, which is characterized by the gradual process of contraction which it undergoes. This is usually known as *cicatricial tissue*.

FIG. 97.



Varieties of new Growth resulting from chronic inflammation of Connective Tissue.—A, an adenoid, B, a fibroid structure. $\times 200$.

The characters of this new tissue present certain variations. Sometimes it consists of closely packed wavy fibres, amongst which are a few elongated spindle-shaped elements, such as are represented in Fig. 97, B. It is equally common for the tissue to assume the appearance shown in Fig. 97, A—a dense homogeneous or obscurely fibrillated material, forming meshes of various sizes, within which are grouped a few lymphoid cells. (See also Fig. 115.) These two varieties are very frequently associated in the same specimen, the former representing a higher degree of development than the latter.

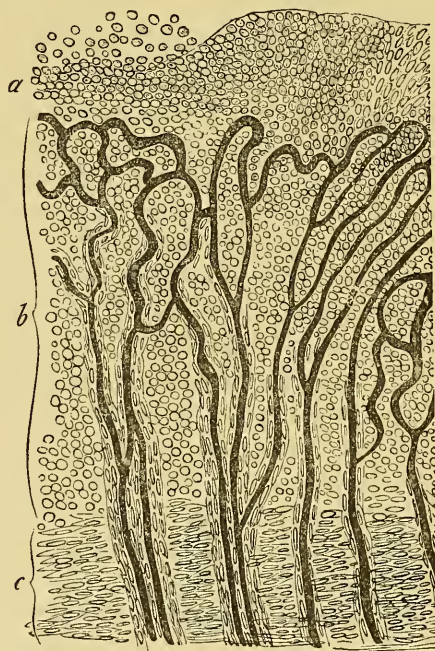
SUPPURATION.—When the inflammatory process is so intense or so prolonged as to prevent the occurrence of resolution or immediate organization, the young cells infiltrate the tissue in such numbers that they may accumulate so as to constitute pus. The pus may either become collected together within the tissue so as to form an abscess, or it may be continuously discharged from the surface, as in a granulating wound. The deleterious influence which the pus exercises upon the tissues with which it comes in contact, causing their destruction and absorption, has already been alluded to. (See “Suppuration.”)

Organization after Suppuration.—This constitutes what is generally known as healing by *granulation*, or by the second intention. It takes place in wounds in which, from the non-apposition of the wounded surfaces, union by the first intention has not been effected; and in other lesions in which the injured tissue presents a free surface, as an ulcer. The process of repair after the separation of a dead

part (demarcation and separation) is in the same way effected by granulation, as is also the closing of the cavity left after the discharge of the contents of an abscess. In all these and similar cases the inflammation and suppuration of the tissue are followed by the formation of granulations, and by the subsequent development of these into a fibrillated structure.

The process of organization in these cases is effected, in the first place, by the development of the young cells in the superficial layers of the inflamed tissue into a granulation-tissue, in the same manner as when there is no suppuration. This granulation-tissue, however, being situated superficially, and not being subjected to pressure,

FIG. 98.



A Granulating Surface.—*a.* Layer of pus. *b.* Granulation-tissue with loops of bloodvessels. *c.* Commencing development of the granulation-tissue into a fibrillated structure. $\times 200$. (Rindfleisch.)

becomes arranged in the form of small papilliform nodules, which are known as *granulations*. This arrangement of the granulation-tissue in the form of granulations appears to be determined by that of the new capillary bloodvessels which are developed so rapidly in it.

These vessels form little vascular loops, and the young cells are arranged around them so that each loop corresponds with a single granulation. The deeper layers of the granulation-tissue gradually become developed into a fibrillated structure, whilst the cells on the surface of the granulations, together with the liquids exuded from the subjacent vessels, are discharged in the form of pus. (Fig. 98.)

CHAPTER XXXVI.

INFLAMMATION OF BONE.

INFLAMMATORY processes in bone give rise, for the most part, to an increase of medullary tissue, and to softening of the compact osseous structure.

The process takes place in the medullary tissue and in the Haversian canals, the primary vascular phenomena being accompanied by an abundant emigration of blood-corpuscles. The cells in the medullary spaces and Haversian canals also undergo changes. In those which contain fat--the adipose cells--the fat is absorbed. Some of the cells enlarge and their nuclei multiply, and thus are produced large multinucleated elements (myeloid cells), similar to those usually met with in growing bone. Whether there is any new cell-formation is uncertain. As the result of these changes, the medullary spaces become occupied by a richly-cellular tissue.

Whilst these changes are taking place in the medullary tissue, the surrounding osseous lamellæ are gradually absorbed, the lime salts are removed, and in this way the medullary spaces and Haversian canals increase in size, and ultimately become confluent. There is thus a new formation of medullary granulation-tissue at the expense of the compact osseous structure, and the bone becomes exceedingly spongy, soft, and vascular.

If the process be not severe it may occasionally, in its earliest stage, terminate in resolution. More commonly, however, it continues until more or less of the bone becomes replaced by the inflammatory tissue. If the inflammation be of considerable intensity it

leads to the formation of pus. The cellular infiltration increases, the compact osseous tissue becomes more and more absorbed, and the pus which is produced may accumulate beneath the periosteum or in the centre of the bone, so as to form an abscess. This constitutes the condition known as *osteo-myelitis* or *acute ostitis*. These intense forms of inflammation often lead to necrosis of the bone.

When the inflammation is of much less intensity, the new inflammatory tissue may undergo progressive development, and form new bone. In this case a new formation of osseous tissue takes place in the enlarged Haversian canals and cancellous spaces, so that the bone becomes converted into a heavy dense structure, consisting of hard compact osseous, with very little cancellous, tissue. This is *sclerosis* of bone.

PERIOSTITIS.—Inflammation of the periosteum may be localized or diffuse, acute or chronic. Acute inflammations of the periosteum lead to the formation of pus, which accumulates between the bone and the periosteal membrane. This, by interfering with the vascular supply, frequently causes necrosis of the superficial layers of the bone; and if a large portion of the periosteum be involved, and the inflammatory process extend to the deeper parts of the bone, the whole bone may die. Another not infrequent result of periostitis is a chronic superficial inflammation and caries of the bone.

When the inflammation of the periosteum is less intense and more chronic, the new inflammatory growth produced in the deeper layers of the membrane may become developed into osseous tissue (periosteal ossification).¹ The process thus causes enlargement of the bone, or if this be necrosed, it helps to reproduce the lost structure. (See "Necrosis.")

Strictly localized inflammations of the periosteum occur in the formation of nodes, and here also there is frequently a new growth of bone.

NECROSIS.—All conditions interfering with the supply of blood to a bone may be causes of its death. Necrosis may thus result from accident, portions of bone being violently separated from their vascular connections, or, more commonly, the periosteum being stripped off and injured. Much more frequently, however, it is the result of the

¹ According to Billroth, this new osseous tissue is partly derived from the bone itself, which, he states, is the seat of a superficial ostitis. (See "Billroth's Surgical Pathology and Therapeutics," translated by Hackley. 4th edit., p. 419.)

intense inflammatory processes in the bone or periosteum which have been described.

The bone, when dead, undergoes a gradual process of separation from the adjacent living tissue. This is effected in the same way as the separation of soft structures. (See "Necrosis.") The adjacent living bone becomes the seat of an inflammatory process, a granulation-tissue and pus are produced, and by this means the dead portion is completely separated. When separated it is termed a *sequestrum*.

The removal of the sequestrum from the granulation-tissue with which it is in contact is often only effected with considerable difficulty, especially if it be deeply seated. This difficulty is occasionally due to a more or less thick layer of the old bone surrounding the necrosed portion. Much more frequently, however, it is owing to the participation of the periosteum in the inflammatory process. The inflamed periosteum produces new bone, a capsule of which is thus formed, inclosing the sequestrum. Openings exist in this capsule (*cloacæ*) leading to the dead bone, and through these openings the inflammatory products are discharged. When the sequestrum is quite superficial, its removal is, of course, more readily effected.

CARIES.—By caries is understood that inflammatory disintegration of bone and removal of the dead products which corresponds with ulceration of soft parts. Caries is therefore one of the results of inflammation of osseous tissue.

Inflammatory processes in bone which are of comparatively slight intensity have been seen to be characterized histologically by a gradually increasing production of an inflammatory granulation-tissue from the medullary tissue of the bone, and by the absorption of the compact osseous structure. This absorption of the bone appears to be effected entirely by the new inflammatory growth. When these chronic inflammatory processes occur in the superficial layers of the bone beneath the periosteum, the bone is gradually destroyed, and presents a ragged, irregular, excavated surface. This is superficial caries, or ulceration of bone. The floor of the ulcer consists of a cancellous structure containing the débris of the disintegrating process. In many cases there is a marked condensation (sclerosis) of the deeper portions of the bone.

Chronic inflammatory processes in the interior of bone cause in the same way absorption and disintegration of the osseous structure. Here, however, the inflammatory products being less readily removed, sometimes undergo, especially in scrofulous children, a kind of caseous

transformation, and the carious cavity contains molecular debris, sanious pus, and minute portions of dead bone. The inflammatory granulation-tissue often projects as fungating masses into the cavity.

Caries is frequently associated with more or less necrosis, especially when the process affects the interior of the bone. Small portions of bone are cut off from their vascular supply, become detached, and are found in the carious cavity.

There are two other morbid conditions of bone, which although probably not coming within the category of inflammation, may be conveniently described in the present chapter—viz., *Mollities Ossium* and *Rickets*.

Mollities Ossium.

Mollities Ossium or Osteomalacia is a rare disease, occurring only in adults. It is characterized by a progressive softening of the bones, owing to an increase in their medullary tissue and the destruction of the compact osseous structure. The bones become so much softened that they can be easily cut with a knife; they are exceedingly light, and bend readily in all directions. On section, the cortical layer is found to be almost destroyed, the bone consisting of a wide cancellous structure containing a reddish, gelatinous, fatty material.

The nature of the disease is obscure. According to Rindfleisch, the change consists in a decalcification of the osseous tissue spreading gradually from the medulla and cancelli of the bone. The decalcified tissue does not become so completely absorbed as in inflammation of bone, but undergoes more or less of a mucoid change. The medullary tissue is exceedingly vascular, but unlike ordinary granulation-tissue it usually contains much fat. Lactic acid has been found in the bone and in the urine. The urine usually also contains lime salts, which have been removed from the bone and eliminated by the kidneys.

Rickets.

The common disease of children so well known as Rickets, or Rachitis, is mainly characterized by certain alterations in the bones. The bones generally are softened. The ends of the long bones are enlarged, and the flat bones are thickened. As a result of these alterations the bones become deformed, and their growth is frequently arrested.

Respecting the nature of this disease, we are at present unable to speak certainly. It appears, however, to be closely associated with

mal-nutrition, and all those conditions which materially interfere with the nutrition of the child may be causes of the disease.

The alteration in the bones may be briefly described—as stated by Sir W. Jenner—as consisting in an increased preparation for ossification, but an incomplete performance of the process. In a growing bone the zone of soft tissue in which the process of conversion of cartilage into bone is taking place is exceedingly narrow, the changes in the cartilage involving only one or two rows of the cartilage cells. In rickets this transition zone is very considerably widened, the changes in the cartilage cells extending for some depth into the cartilage, and the adjacent layer of cancellous tissue being much broader than natural. The junction between the bone and the cartilage is also exceedingly irregular, so that in some parts the cancellous bone extends into the cartilage much further than in others. Usually the alterations in the cartilage in the transition zone are accompanied by the calcification of the new tissue and its conversion into bone. In rickets, however, this calcification takes place very incompletely, and thus a wide layer of imperfectly calcified soft tissue is formed at the growing end of the bone.

A similar abnormality exists in the process of ossification from the periosteum. Here also the zone of vascular granulation-tissue from which the bone is developed is exceedingly broad, the calcification of the tissue is exceedingly incomplete, and the bone thus becomes thickened by a soft, vascular, and very imperfectly calcified structure. As the bone grows the medullary cavity naturally widens, and the compact tissue becomes absorbed. This imperfect formation of osseous tissue from the periosteum produces, therefore, considerable softening and weakening of the bone.

The changes in the bones in rickets thus closely resemble those which occur in the normal process of ossification. There is the same change in the cartilage cells and in the deeper periosteal layers, but this change involves abnormally large areas. The development of the young cells and the transformation of the new tissue appears also to be more or less incomplete. In many parts the young elements do not form perfect bone-cells, but simply angular cells without canaliculi, whilst in others the development may be much more complete. Various transitions are thus met with between tolerably well-developed and very imperfect bone-structure, but owing to the deficiency of lime salts this structure is very imperfectly and very irregularly calcified.

CHAPTER XXXVII.

INFLAMMATION OF BLOODVESSELS.

Inflammation of Arteries.

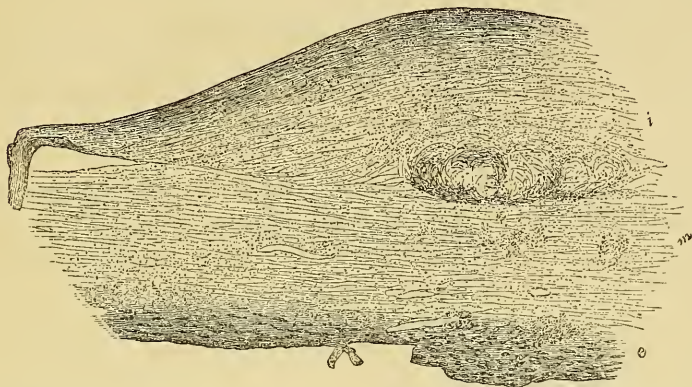
IN studying the process of inflammation in arteries, it must be borne in mind that the inner coat of these vessels is non-vascular, the bloodvessels being distributed in the external layers.

Acute and chronic inflammations of arteries are a very frequent result of coagulation of the blood within the vessel (thrombosis). Such inflammations have been considered in the chapter on Thrombosis. Independently of thrombi, the most acute inflammatory processes in arteries are for the most part the results of injuries from violence, or of inflammation in adjacent tissues. Here, the histological changes are principally confined to the *external* coat of the vessel. This becomes exceedingly hyperæmic and infiltrated with small cells, the cellular infiltration involving also the middle coat. As a consequence of these changes in the outer coats the vitality of the intima may be impaired or destroyed, and when this has occurred the blood contained within the vessel coagulates.

ATHEROMA.—The more chronic forms of arterial inflammation give rise to changes which are most marked in the deeper layers of the *inner* coat, where they produce those various alterations in the walls of the vessel included under the common term—*atheroma*. In the earliest stage of the inflammatory process the fibrous and elastic lamellæ of the inner coat of the vessel become infiltrated with small cells, which are probably partly emigrants, and partly derived from the cells of these structures. As these cells increase in number they give rise to a swelling beneath the innermost layers of this coat or the artery. (Fig. 99.) This swelling of the intima is very characteristic. It is, in the early stage of the process, of a soft flabby consistence, and the lining membrane which is continuous over it can be stripped off, leaving the diseased tissue beneath. It thus contrasts strongly with the superficial patches of fatty degeneration which result

from the fatty metamorphosis of the endothelial and connective-tissue cells of the vessel. (See "Fatty Degeneration of Arteries.")

FIG. 99.



Atheroma of the Aorta.—Showing the cellular infiltration of the deeper layers of the inner coat, and the consequent internal bulging of the vessel. The new tissue has undergone more or less fatty degeneration. There is also some cellular infiltration of the middle coat. *i.* internal, *m.* middle, *e.* external coat of vessel. $\times 50$, reduced $\frac{1}{2}$.

The results of the inflammatory process will depend upon its severity. If the process be very intense, the young elements accumulate rapidly and infiltrate the middle and external coats, so that the walls of the vessel become so much softened, that dilatation, aneurism, or rupture may ensue. Such acute changes are a common cause of aneurism. The inflammation, however, is usually of less intensity and runs a more chronic course, and it is only to these more *chronic* arterial changes that the term "atheroma" is commonly applied.

When the process is less intense and more chronic in its course, it leads to various alterations in the wall of the vessel. The soft cellular infiltration of the deeper layers of the intima usually undergoes retrogressive changes, owing to deficient nutritive supply. These changes commence in the deeper portions of the new tissue. The young cells undergo fatty degeneration, the intercellular substance softens, and thus a soft, yellowish, pultaceous material may be produced beneath the lining membrane of the vessel. This has been termed an *atheromatous abscess*. The lining membrane may ultimately give way and the softened matters be carried away by the circulation, and thus is produced the *atheromatous ulcer*. In other cases the more liquid constituents of the degenerated tissue gradually become absorbed, cholesterin forms, and thus a mass, consisting of broken-

down fibres and cells, fatty débris, and cholesterin crystals, with a varying quantity of the original fibrillated tissue, remains in the deeper layers of the inner coat. (Fig. 99.) This may subsequently calcify, and so form a *calcareous plate*.

In the most chronic forms of the atheromatous process there is more or less fibrillation of the new tissue, and thus is produced a *fibroid thickening* of the inner coat of the artery. The organization, however, is rarely complete, more or less fatty débris being usually inclosed in the fibroid stroma.

Respecting the causes of these chronic arterial inflammations included under the common term of atheroma—they are probably mainly due to over-strain of the vessel, the strain exercising a chronic injurious influence. This view has been especially insisted upon by Dr. Moxon.¹ It is supported by the fact that those vessels which are the most exposed to strain are the most liable to this disease—*e. g.*, the arch of the aorta; also by the exceeding frequency of atheroma in all those conditions in which there is an increase of the blood-pressure. The effect of increased blood-pressure as a cause of atheroma is seen in the liability of athletes to the disease; and also in the frequency with which it occurs in chronic Bright's disease, and in the pulmonary vessels in cases of mitral obstruction, etc. The occurrence of atheroma is also favored by syphilis.

Inflammation of Veins.

Inflammatory processes in veins are more frequent than in arteries, but here they are in the very great majority of cases *secondary* to coagulation of the blood within the vein (thrombosis), the coagulum exercising an injurious influence upon the coats of the vessel. These inflammations resulting from thrombosis have already been described. (See "Results of Thrombosis.")

The inner coat of the veins is, like that of the arteries, non-vascular, and hence acute inflammatory changes are, for the most part, confined to the external and middle coats. Independently of inflammations resulting from thrombosis, the lining membrane of veins appears to undergo no inflammatory changes.

Acute and chronic inflammatory processes in veins are, as already stated, most frequently due to thrombosis. They may also result

¹ "Lectures on Pathological Anatomy." Wilks and Moxon, 2d edit., p. 150.

from violent injury, or from the extension of inflammation from adjacent tissues. The process, when acute, closely resembles that in the arteries. The external and middle coats become infiltrated with cells, the vitality of the intima ultimately becomes impaired or lost, and when this has occurred the blood within the vein coagulates.

CHAPTER XXXVIII.

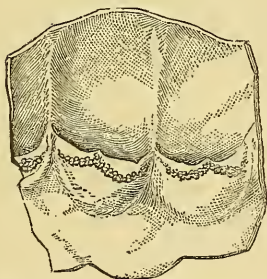
INFLAMMATION OF THE HEART.

INFLAMMATORY processes in the heart may affect the substance of the organ, or the endocardium. They are much more frequent in the last-named situation.

Endocarditis.

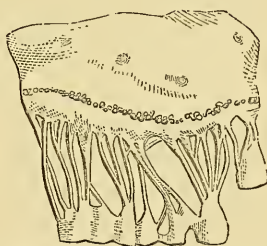
Endocarditis is for the most part limited to the valves of the heart, although it is occasionally met with involving more or less of the

FIG. 100.



Inflammation of Aortic Valves.—The earlier stage of the process. Showing the situation of the inflammatory granulations.

FIG. 101.

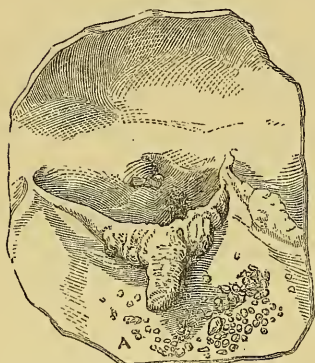


Inflammation of Mitral Valve.—The earlier stage of process. Valve seen from the auricular surface. Showing the situation of the inflammatory granulations.

cardiac cavities. The process is almost exclusively confined to the *left* side of the organ, and in the great majority of cases it commences in, and comparatively rarely extends beyond, the confines of the aortic and mitral valves and corresponding orifices. Further—it is

those portions of the valves which come into contact in the act of closure, and are thus *most exposed to friction*, which are especially involved, and in which the changes usually commence. Thus, in the aortic valves, it is the convex surfaces of the segments which are most liable to be affected, and not the free edge of the segment, but the little band of tissue which passes from its attached border to the corpus Arantii in the centre (Fig. 100); and in the mitral valve, the

FIG. 102.



Endocarditis due to Friction.—The drawing represents a long vegetation on one of the segments of the aortic valve, which by rubbing on the endocardium below has produced numerous inflammatory granulations (A).

auricular surface of the segments at a little distance from the attachment of the chordæ tendineæ (Fig. 101). When portions of the endocardium apart from the valves are affected, this is frequently due, as pointed out by Dr. Moxon, to the irritation caused by the friction of vegetations or fibrinous clots situated on the valves themselves (Fig. 102.)

The histological changes accompanying endocarditis resemble those already described as occurring in those more chronic forms of arterial inflammation known as atheromatous. The endocardium and inner coat of an artery are very analogous in their structure, both being non-vascular, and consisting of a layer of connective tissue with an internal endothelial covering. The inflammatory process may be acute or chronic.

ACUTE ENDOCARDITIS.—If the process be acute, the deeper layers of the endocardium become rapidly infiltrated with young cells, and as these increase in number the intercellular substance becomes softened and destroyed, and thus is produced a soft tissue composed almost entirely of cells such as always results from inflammatory processes in connective tissue. The new tissue as it increases tilts up the superjacent endothelium and projects in the form of minute granulations and vegetations upon the surface of the softened valve. (See Figs. 100 and 101.) The endothelial elements probably also participate in the active process.

The above changes take place in an almost non-vascular tissue, and although there is more or less increase of vascularity in the more external endocardial layers, where the capillaries are more numerous,

there is rarely any redness or injection of the endocardium seen after death. Neither is there usually any liquid exuded upon the surface of the granulations. What was formerly regarded as an exuded material, is in the main coagulum which has been deposited from the blood upon the roughened surface of the valve. This deposition of coagulum frequently occurs in endocarditis, the roughened and abnormal endocardium acts as a foreign body and so causes a deposition upon its surface. This must not be confounded with the vegetations themselves.

(Fig. 103.)

The results of this cellular infiltration vary. If the process be very intense the new tissue may break down and thus a loss of substance result—an endocardial ulcer. This takes place without any accumulation of cells sufficient to form an abscess, the new tissue simply becoming rapidly softened and disintegrating. In rare cases, however, small quantities of pus are found in the deeper endocardial layers. The ulcer is irregularly defined, and its edges are usually swelled and thickened. This *ulcerative endocarditis* is, however, not frequent, the process usually being less acute. The ulceration may lead to perforation of the valve, or to a considerable destruction of its substance. Laceration or aneurism of the valve may also ensue from the pressure exercised by the blood against the damaged tissue. Sometimes the ulcerative process extends so as to involve the cardiac substance. Ulcerative endocarditis is a grave affection, often giving rise to embolism, and sometimes to a pyæmic process.

When the inflammatory process is less intense, as is much more commonly the case, the new tissue becomes incompletely organized into a fibrillated structure, whilst it undergoes, in part, fatty and calcareous degeneration. These changes may result in the adhesion of the valves, either to one another or to the walls of the heart. They always produce permanent *thickening, rigidity, and shrinking* of their structure. The new tissue may continue to grow after the severity of the process has subsided, and thus are produced the vegetations and papillary excrescences on the valve which are so commonly met with. (See Fig. 102.) These consist of a lowly organized tissue, which tends to undergo fatty and calcareous changes.

FIG. 103.



Acute Endocarditis.—A granulation from the mitral valve, showing a fibrinous coagulum upon the surface of the granulation. $\times 10$ (Rindfleisch).

CHRONIC ENDOCARDITIS.—This may be the sequel of acute inflammation, or the process may, from its commencement, be chronic in its nature. In chronic endocarditis the cellular infiltration is much less rapid and abundant than in the acute form; the intercellular substance consequently becomes much less softened and destroyed, and the new tissue has a much greater tendency to become developed into a fibrillated structure. The result of these chronic processes is therefore to produce a *fibroid thickening* of the endocardium, and so to cause considerable induration and contraction of the valves or valvular orifices. The new tissue sometimes forms papillary growths on the valves, which undergo partial fatty and calcareous changes. (See Fig. 102.)

Myocarditis.

Myocarditis, or inflammation of the cardiac substance, is much less frequent than the preceding. Intense and concentrated inflammations leading to the formation of abscess probably occur only as the result of a pyæmic process. Less intense and more diffuse forms of cardiac inflammation are also not unfrequently met with in association with

FIG. 104.



Acute Myocarditis.—From a case of acute rheumatism. *a.* A thin section of the left ventricle made in the direction of the muscular fibres, showing the granular and swollen condition of the fibres, and the prominence of their nuclei. *b.* A transverse section, showing the cellular infiltration of the intermuscular tissue. $\times 200$.

pericarditis, and, less commonly, with endocarditis. Here the inflammatory process appears, by extension, to involve the immediately adjacent muscular layers of the organ, which are found infiltrated with small cells, the fibres themselves being softened and granular.

In addition to the above, a form of myocarditis must be recognized in which the substance of the heart becomes more generally involved. In certain cases of acute rheumatism the muscular tissue of the heart is found after death swollen, softened, opaque, and occasionally faintly mottled with slightly yellowish patches. When examined microscopically, the fibres are seen to have lost their striation and to be finely granular, their nuclei are large and prominent, and small cells are found in varying numbers, infiltrating the intermuscular tissue. (Fig. 104.) I have met with these appearances in two or three cases of acute rheumatism, and they must, I think, be regarded as evidence of the existence of an acute inflammatory process. The change is most marked in the left ventricle, and it is usually associated with endo- or peri-carditis. It is a grave complication of acute rheumatism, and possibly of some other diseases, and is probably more frequent than is generally supposed.

FIBROID INDURATION OF THE HEART.—This, a comparatively rare condition, is probably, in most cases, a result of myocarditis. The change is characterized by the development of a fibrillated tissue between the muscular elements. The process commences in the inter-

FIG. 105.



Fibroid Induration of the Heart.—A thin section from the wall of the left ventricle, showing the small-celled growth in the intermuscular septa around the bloodvessels. *a. a.* vessels. $\times 200$.

FIG. 106.



Fibroid Induration of the Heart.—A section from the left ventricle of the same heart as Fig. 105, showing a more advanced stage. The fibroid tissue surrounds the individual muscular fibres, which are undergoing fatty degeneration. $\times 200$.

muscular septa around the bloodvessels. This becomes infiltrated with small cells, which tend to become developed into a fibrillated structure. (Fig. 105.) The growth of new tissue gradually extends between the bundles of muscular fibres, so that ultimately each fibre may be surrounded by a tract of dense fibroid tissue. (Fig. 106.) The muscular fibres themselves, owing to the resulting interference

with their nutritive supply, atrophy, undergo fatty metamorphosis, and are gradually replaced by the fibroid growth. (Fig. 106.) Very frequently the cellular nature of the growth, which I believe to characterize the earlier stages of its development, is not seen, the new issue being simply fibroid.¹

Fibroid induration of the heart appears in most cases to be induced by inflammatory processes commencing in the peri- or endo-cardium. When secondary to pericarditis, the change is usually most advanced in the more external portions of the cardiac walls, and it commonly affects both the right and left ventricles. When, on the other hand, an endocarditis is the precursor of the indurative process, the change is more marked in the internal muscular layers, and inasmuch as inflammatory processes in the endocardium occur almost exclusively in the left cardiac cavities, the left ventricle is principally involved. In other cases the fibroid growth appears to be the result of syphilis. (See "Syphilis.")

Although the growth of new tissue is thus usually more advanced in certain portions of the muscular walls than in others, it is by no means uniformly distributed. In some parts it may be very dense, the muscular fibres being entirely obliterated, whilst in others it is entirely wanting, and the muscular elements present a normal appearance.

Fibroid induration of the heart—excluding that resulting from syphilis—appears to occupy the same pathological position as similar fibroid changes in other organs—*e. g.*, in the liver and kidneys. It must therefore be regarded as the result of a chronic inflammatory process—a chronic myocarditis. Its effect must evidently be to interfere very materially with the motor power of the organ, and it consequently constitutes one of the most grave of all the cardiac diseases.

The cardiac walls may become much thickened by the new growth, and the induration of texture is often very considerable. In the specimen from which the accompanying drawings were made the walls of the left ventricle were so hard that they cut almost like a piece of tendon.

¹ Dr. Hilton Fagge, in a series of eleven cases of fibroid disease of the heart, found that cellular elements in the new growth were almost invariably absent. (See *Trans. Path. Soc. Lond.*, vol. xxv. p. 64.)

CHAPTER XXXIX.

INFLAMMATION OF LYMPHATIC STRUCTURES.

INFLAMMATORY processes in lymphatic structures usually result from their injury by substances conveyed to them by the lymphatic vessels. They include—*acute* and *chronic* inflammations, and the specific inflammations associated with *Typhoid Fever*. Each of these must be considered separately.

Acute Inflammation of Lymphatic Structures.

Examples of acute inflammation of lymphatic structures are furnished by the inflammation of the glands in the axilla from a wound on the hand, of the glands in the groin from gonorrhœa, and of Peyer's and the solitary glands in the intestine from inflammation of the intestinal mucous membrane.

The process consists in a hyperæmia of the gland together with a rapid increase in the number of the lymph-cells. This increase is probably due, partly to a hyperplasia of the original cells of the gland, and partly to the migration of blood-corpuscles. The cells not only increase in number, but many of them become much larger in size, and their nuclei multiply. The cells of the trabeculæ also participate in the active process. The increase in the size of the elements and the multiplication of their nuclei usually leads to the production of some larger cells containing two or three nuclei. These have been already alluded to as being frequently met with in lymphatic structures which are undergoing active processes. (See Fig. 38.) Owing to these changes the gland becomes considerably increased in size, soft and pulpy in consistence, and its cortical and medullary parts are no longer distinguishable.

Upon the removal of the injurious influence the process may gradually subside, the new elements undergo disintegration and absorption, and the gland returns to its normal condition (Resolution).

In other cases the process goes on to suppuration, the trabeculæ are destroyed, many of the cells become disintegrated, and the loculi

of the gland become filled with pus. This is usually associated with inflammation and suppuration of the surrounding connective tissue. In the glands of a mucous membrane the process gives rise to what is known as a follicular abscess.

Chronic Inflammation of Lymphatic Structures.

Chronic Inflammations of lymphatic structures result from injuries which are less severe and more prolonged in their action than those which give rise to the acute form. The resulting cellular infiltration of the gland is consequently a more continuous one, and the gland

FIG. 107.



Chronic Inflammation of a Lymphatic Gland.—Showing the increase in the stroma, and the diminution in the number of the lymphoid cells. $\times 200$.

becomes more or less permanently increased in size. The reticulum is also considerably involved. These chronic inflammatory processes differ from the acute, inasmuch as they lead to a gradually increasing development of the reticular structure of the gland. The reticulated network becomes thicker and more fibrous, its meshes become smaller and smaller, the lymph-cells diminish in number, and thus the gland becomes hard and fibrous in consistence. (Fig. 107.)

Scrofulous Glands.—In those chronic inflammations of the lymphatic glands which occur in scrofulous subjects, and in which the glands tend to become caseous, the changes resemble those which have been already described as characteristic of scrofulous inflammation. (See “Scrofulous Inflammation.”) The cellular infiltration is considerable, there is but little tendency to absorption, and many of the cells increase in size, and even form multinucleated elements. The gland thus becomes enlarged, soft, and elastic in consistence, and of a uniform grayish-white color. Owing to the obstruction to the circulation caused by the pressure of the cellular infiltration, the gland undergoes retrogressive changes and becomes caseous. The caseous material may subsequently liquefy, or become infiltrated with calcareous particles. Many caseous lymphatic glands are tuberculous (see “Tuberculosis of Lymphatic Glands”).

Inflammation of Lymphatic Structures in Typhoid Fever.

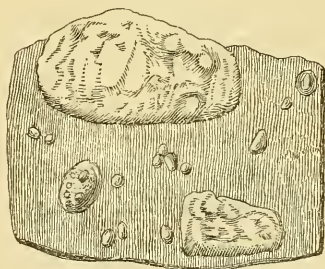
The inflammatory processes which occur in the lymphatic structures in Typhoid Fever have their seat in the spleen, in the lymphatic structures of the intestine, and in the mesenteric glands.

The Spleen.—In the spleen the change resembles that which occurs in many of the other acute febrile diseases, although it reaches its maximum in typhoid. The splenic tissue becomes exceedingly vascular and the lymphatic elements increase rapidly in number, so that the organ often attains two or three times its natural size. Many of the new elements enter the blood, thus causing a slight temporary increase in the number of white blood-corpuscles. As the fever subsides, the hyperæmia diminishes, many of the new elements undergo disintegration and absorption, the remainder enter the blood, and thus the organ again attains its normal characters and dimensions.

The Intestinal Lymphatic Structures.—It is in the solitary and Peyer's glands that the most characteristic changes take place in typhoid fever. These structures may be involved throughout the whole of the small and large intestine, but in most cases the process is limited to those in the ileum and cæcum; and those glands are always the most affected which are situated the nearest to the ileo-cæcal valve.

The primary change here consists in a hyperæmia and cellular infiltration of the glands. Many of the cells increase considerably in size, so as to form the multinucleated elements already alluded to. Both Peyer's patches and the solitary glands thus become considerably enlarged and prominent, standing up above the surface of the intestine. (Fig. 108.) They are of a grayish-white or pale reddish color, and of a soft, brain-like consistence. The surrounding mucous membrane is also exceedingly vascular, and is the seat of an acute catarrhal process. This catarrh is more or less general, and usually precedes the swelling of the glands. The cellular infiltration, in many parts, rapidly extends beyond the confines of the glands into the immediately surrounding

FIG. 108.



Typhoid Swelling of Peyer's Patches and Solitary Glands of the Intestine.

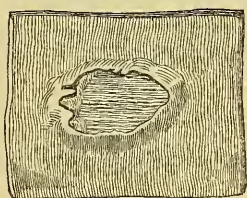
and subjacent tissues, and even in some cases into the muscular coat.

The process now passes into the second stage—that of the death and disintegration of the newly formed tissue. This may terminate in various ways. The enlarged glands, many of them, subside, the new elements become disintegrated and are absorbed, and the gland thus undergoes a gradual process of *resolution*. In others, the individual follicles of the gland rupture, discharging their contents externally, and the patches then acquire a peculiar reticulated appearance. The most characteristic termination, however, of the typhoid process, is the separation of the dead tissue as a slough, and the formation of the *typhoid ulcer*.

The process of sloughing and ulceration may, like the cellular infiltration, take place uniformly throughout the whole gland, in which

case the whole mass is thrown off, leaving an ulcerated surface corresponding in size with that of the gland. (Fig. 109.) More commonly, however, in the patches, the sloughing commences in different portions of the patch, and small irregular losses of substance result, which may gradually extend until they form one large ulcer.

FIG. 109.



A Typhoid Ulcer of the Intestine.

Although, as already stated, the cellular infiltration may extend beyond the confines of the glands, this is rarely the case with

the ulceration. The peripheral infiltration undergoes resolution, and hence the ulcers have the same configuration as the original glands; those originating from the patches being oval, with their long diameter in the direction of the gut; and those originating in the solitary glands being spherical in shape. In rare cases, when there is much

infiltration of the surrounding mucous membrane, the ulceration may extend slightly beyond the confines of the glands.

FIG. 110.



A Typhoid Ulcer of the Intestine (diagrammatic).—Showing the undermined edges of the ulcer and the slough still adherent. *a.* Epithelial lining. *b.* Submucous tissue. *c.* Muscular coat. *d.* Peritoneum.

edges of the ulcer. The base is smooth, and is usually formed of the submucous or muscular coat of the intestine. The edges are

With the sloughing and disintegration of the new tissue the process of infiltration ceases, and hence there is no induration or thickening of the base or

thin and undermined, and consist of a well-defined fringe of congested mucous membrane. (Fig. 110.) This is best seen when the gut is floated in water. In some cases, however, the sloughing extends deeper through the muscular layer to the sub-peritoneal tissue, and it may thus cause perforation and peritonitis.

The third stage of the process is that of cicatrization. This takes place by the resolution of the peripheral infiltration, the approximation and union of the undermined edges with the floor of the ulcer, and the gradual formation from the margin of an epithelial covering. The gland-structure is not regenerated. The resulting cicatrix is slightly depressed, and less vascular than the surrounding mucous membrane. There is no puckering or diminution in the calibre of the gut. In some cases, however, cicatrization does not take place so readily, and the floor of the ulcer becomes the seat of a *secondary* ulceration. This usually takes place after the general disease has run its course, or during a relapse. Profuse hemorrhage and perforation more commonly result from the secondary ulceration than from the primary sloughing of the glands.

The Mesenteric Glands.—The change in the mesenteric glands is probably secondary to that in the intestine. These glands become the seat of an acute cellular infiltration, and are enlarged, soft, and vascular. They usually, like many of the glands in the intestine and the spleen, undergo a gradual process of resolution. In rare cases, however, the capsule of the gland is destroyed, and the softened matters may escape into the peritoneal cavity and so cause peritonitis. The enlarged glands may also become caseous, and subsequently calcified.

CHAPTER XL.

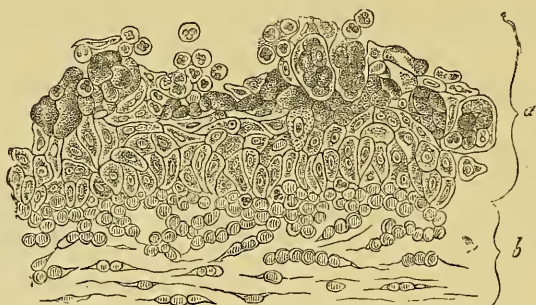
INFLAMMATION OF MUCOUS MEMBRANES.

IN mucous membranes inflammatory processes are divided into *catarrhal*, and *fibrinous*, *croupous*, or *diphtheritic* inflammation.

CATARRHAL INFLAMMATION.—Catarrhal inflammation, or as it is more commonly called *catarrh*, is much the more frequent. In its milder forms this is characterized mainly by an increased secretion of

mucus. The initial hyperæmia of the membrane is followed by an abnormal production of epithelial and mucous elements. The liquid which transudes from the bloodvessels is more abundant, the small spherical cells which constitute the mucus-corpuscles are produced with increased rapidity, and the result is an increased secretion of mucus, rich in cellular elements. These young cells are most of them emigrant blood-corpuscles, others are probably the products of epithelial proliferation. As the process continues, some of the epithelial elements become loosened and are discharged with the mucus, and within these groups of bodies may occasionally be seen, which are evidently young mucus-corpuscles. (Fig. 111.) How far these are white blood

FIG. 111.



Catarrhal Inflammation of the Conjunctiva.—*a.* Epithelium. *b.* Sub-epithelial connective tissue.—Showing the proliferation of the epithelium, and the young elements within the epithelial cells. (Rindfleisch.)

corpuscles which have penetrated the epithelial cells is at present uncertain. The secretion of the mucous glands is also increased. Owing to these changes, the mucous membrane becomes swelled and abnormally vascular. The increased vascularity is evidenced by redness during life, but after death the blood usually passes out of the vessels, and the membrane may look paler than natural.

If the inflammation be more intense, the vascular phenomena are more marked, the production of young elements is more rapid, they are smaller and not so well developed, and the secretion becomes puriform from the great number of cellular elements which it contains. It now no longer yields mucin. Many of the elements are indistinguishable from pus-corpuscles, others are somewhat larger and resemble the corpuscles of normal mucus. Between the corpuscles of mucus and pus there is no line of demarcation, the one passing by insensible gradations into the other. The former are somewhat larger

and more regular in shape than the latter, and usually contain only a single nucleus. As the process continues, the sub-epithelial tissue is gradually involved, and becomes infiltrated with small cells. Owing to loss of epithelium, the surface of the membrane may present some slight irregular abrasions.

These changes in the mucous membrane itself are accompanied by inflammation of the lymphatic structures which it contains. The lymph-follicles become enlarged. Their contents may soften and form a minute pseudo-abscess, and this bursting gives rise to a small ulcer. These are the follicular ulcers so often seen in catarrhal conditions of the intestines and pharynx. The ulceration in some cases extends beyond the confines of the follicle. The proper glandular structures may also become involved. Their epithelium multiplies, the glands become choked with the epithelial elements, and they may subsequently atrophy. This is seen in catarrh of the stomach.

The acute process may quickly subside, or it may become chronic. In the latter case the hyperæmia diminishes, but the escape of leucocytes and the multiplication of the epithelial elements continue, and the sub-epithelial tissue becomes more extensively infiltrated with small cells.

Chronic catarrhal inflammations of mucous membranes differ from the acute, inasmuch as the sub-epithelial connective tissue is much more extensively involved. This tissue becomes infiltrated with small elements, which may ultimately form an imperfectly fibrillated structure. The membrane thus becomes indurated and thickened, and the pressure exercised by the new growth may induce atrophic changes in the glandular structures which it contains; by preventing the exit of their secretion it may also cause them to dilate so as to form cysts. This atrophy of the proper glandular structures is seen in chronic catarrh of the stomach. These changes in the sub-epithelial connective tissue are usually accompanied by enlargement of the lymphatic structures, an enlargement which sometimes gives to the membrane a nodular or granular appearance. This is well seen in the pharynx (follicular pharyngitis). The enlarged lymphatic structures may also constitute the starting-points of an ulcerative process. (See "Tuberculosis of Mucous Membranes.") In some situations, as the stomach and intestine, the membrane often at the same time becomes deeply pigmented.

FIBRINOUS, CROUPOUS, OR DIPHTHERITIC INFLAMMATION.—These terms are applied to those inflammations of mucous membranes which

lead to the production of a so-called false membrane—such as is seen, for example, in croup. The formation of this fibrinous layer upon the surface of the membrane is quite characteristic, and at once distinguishes this form of inflammation from a simple catarrhal process.

The membrane itself, which may exist in little patches or cover a large area of the mucous surface, is usually of a yellowish or grayish-white color, and in consistence varies from a firm and tough to a soft pultaceous material. It is more or less easily separable from the subjacent tissue, which in all cases after its removal is found to have lost its epithelium. In thickness it may vary considerably in different parts. Examined microscopically, it is seen to consist mainly of leucocytes, granular matter, and some altered epithelial elements inclosed in the meshes of a delicate network of finely fibrillated material resembling coagulated fibrin. The fibrinous network is most marked in the deeper layers of the membrane, whereas the superficial part consists principally of leucocytes, altered epithelium often fused together into irregular masses, and adventitious products. The epithelium of the mucous membrane beneath this fibrinous layer is, as already stated, invariably more or less completely wanting; so that the fibrinous layer extends down to the basement membrane. In some cases the fibrinous layer does not extend deeper than this membrane, in which case it can be readily detached; whereas in others it involves the deeper structures, and then is much less easily removed, and when separated leaves an irregular surface owing to the destruction of the inner layers of the mucous membrane. In the former case the process is usually spoken of as *croupous*, in the latter as *diphtheritic*. These differences, however, in the depth to which the mucous membrane is involved, are probably due to differences in the intensity of the process, and also to differences in the structure of the membrane. In those situations where a distinct basement membrane exists, as in the pharynx and respiratory organs, the process is more likely to be superficial than in those where this is not the case, as in the intestines and conjunctiva. (Cohnheim.) If the inflammatory process continues, the membrane after its removal is reproduced, but if it subside, the epithelium is quickly regenerated, and the deeper structures when destroyed are also gradually reproduced.

With regard to the nature of the false membrane—it is mainly due to the coagulation of the inflammatory exudation liquids, the coagulum inclosing the escaped blood-corpuscles and the altered epithelium of the mucous surface. This coagulation was formerly supposed to

result from the large proportion of albumen which the inflammatory exudation contained, the inflammatory process being of greater intensity than that which gives rise to a simple catarrhal process. Although the coagulation of the inflammatory liquids may thus be partly due to the intensity of the process, the investigations of Weigert render it probable that it is mainly owing to the *death of the epithelium*. According to this observer, living epithelium, like endothelium, prevents the coagulation of the liquor sanguinis, but dead epithelium will cause coagulation of liquor sanguinis in contact with it. The death of the epithelium is usually due to the same injury as that which causes the inflammatory process, but without this necrotic change in the deeper as well as in the superficial epithelial elements, it is probable that an inflammatory process will not be followed by the formation of a so-called false membrane.

The causes of croupous or diphtheritic inflammation are simple mechanical or chemical agencies and injuries of an infective character. Simple mechanical or chemical injuries will produce a typical croupous membrane. This may be done experimentally in dogs, for example, by the application of strong acids, alkalies, or alcohol to the trachea. In cases of poisoning by the mineral acids, and in the accident so common in children of attempting to drink out of a vessel containing boiling water, a false membrane is often produced on the injured mucous surface. In the intestinal and other mucous membranes also a croupous inflammation is sometimes met with as the result of mechanical injury, as for example, in the vermiform appendix from the irritation of a concretion.

More common, however, than these mechanical and chemical causes are injuries of an infective nature, and it is to *infective* agencies that croupous inflammations are most frequently due. As examples of such are some forms of severe conjunctivitis, the intestinal inflammation in epidemic dysentery, and, above all, the changes in the pharyngeal and laryngeal mucous membranes in the diseases known as *croup* and *diphtheria*. These infective croupous processes are almost invariably contagious, the inflammatory products being capable of inducing similar processes when applied to other mucous surfaces. Micrococci appear to be usually present in the false membrane in these infective cases. They are usually found as colonies of globular organisms in the upper layers of the membrane. Whether they are essential or merely accidental is at present uncertain.

Although there are these important differences in the etiology and

nature of croupous inflammations, they are not accompanied by any corresponding variations in the histology of the process; the slight differences met with in the characters of the false membrane and in the extent of implication of the mucous surface being probably usually due to differences in the intensity of the process and in the structure of the mucous membrane involved.

Dysentery.

The inflammatory processes occurring in the intestine in dysentery are for the most part limited to the large intestine, although the ileum is also occasionally involved. The inflammation is always most marked in the rectum and descending colon, and it may be stated generally, that it is characterized by the ulceration and sloughing of the membrane to which it gives rise.

The intestinal changes vary considerably, according to the intensity of the inflammatory process. In the milder forms of the disease the changes are most marked on the summits of the folds of the mucous membrane. These are found covered with a grayish-white layer of fibrinous-looking material, which, when scraped off, leaves a superficial loss of substance. The mucous membrane generally is hyperæmic and softened. The submucous tissue is also infiltrated with inflammatory products, and the solitary glands are enlarged and prominent.

When the process is more severe, the submucous tissue becomes more extensively involved, and the superficial layer of fibrinous material extends over wider areas and implicates more deeply the mucous membrane. The thickening of the intestinal wall, however, is much greater in some parts than in others, so that projections are produced upon the inner surface of the intestine, corresponding with those parts which are the most affected. The enlarged solitary glands usually slough, and so give rise to circular ulcers, which rapidly increase. When the process has reached this stage, the muscular and serous coats are implicated, the latter being covered with layers of fibrin which form adhesions with adjacent parts. The intestine is much dilated, and contains blood and disintegrating inflammatory products.

In the most intense forms of the disease, the necrosis is more extensive. According to Rokitsansky, large portions of the mucous membrane are converted into black rotten sloughs. The submucous

tissue is infiltrated with dark blood and serum, but subsequently it becomes the seat of a reactive suppurative inflammation, by means of which the necrosed portions of tissue are removed.

If death does not occur and the inflammatory process subsides, the ulcers may gradually heal. When the loss of substance has not been considerable, the edges of the ulcers may, by the contraction of the submucous tissue, become completely approximated. More commonly, however, the loss of substance is so great, that portions of the membrane are left, consisting simply of connective tissue.

When the inflammatory process becomes chronic, the changes in the submucous connective tissue become more marked, and the new fibroid growth gives rise to considerable thickening and induration of the intestinal wall, and to more or less contraction and narrowing of the cavity. Sometimes it forms fibrous bands which project into the gut. The formation of abscesses and fistulous passages occasionally occurs in the thickened intestinal wall.

CHAPTER XLI:

INFLAMMATION OF SEROUS MEMBRANES.

INFLAMMATORY processes in serous membranes vary in their intensity, and in the amount and character of the effusion.

The process commences, as in mucous membranes, with hyperæmia, exudation of liquor sanguinis and emigration of blood-corpuscles, together with increased activity of the endothelial elements: The endothelial cells enlarge and become more granular, their nuclei divide, and new elements are formed by endogenous multiplication. (Fig. 112.) The number of new cells which are thus produced, together with some of the older cells, and a large number of emigrant blood-corpuscles,

FIG. 112.

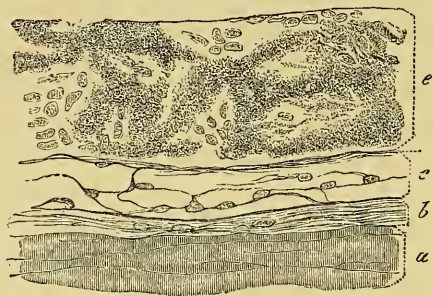


Inflamed Epiploon of a Rabbit.— Showing the endogenous proliferation of the endothelium. $\times 250$. (Cornil and Ranvier.)

escape with the exuded liquor sanguinis into the serous cavity, where they may probably continue to exhibit their formative activity.

Owing to these changes the membrane loses its natural smooth and glistening appearance, and becomes opaque, roughened, and exceedingly vascular. Its surface at the same time becomes covered with a fibrinous layer, and more or less liquid transudes into its cavity. The coagulable material which exudes from the vessels forms a soft, elastic, membranous, or reticulated investment, inclosing in its meshes numerous small cells. This either glues the two surfaces of membrane together, or, if they are separated by liquid effusion, forms a slightly adherent layer. (Fig. 113.) The exuded liquid varies

FIG. 113.



Inflammation of the Diaphragmatic Pleura.—Showing the adherent fibrinous layer. *a.* Muscular coat of diaphragm. *b.* Sub-serous tissue. *c.* Serous membrane. *e.* Fibrinous layer. \times 400. (Rindfleisch.)

considerably in amount and is always turbid, thus differing from non-inflammatory effusions. It contains flakes and masses of coagulated fibrin and innumerable cell-structures, the latter being in the earliest stages of the process almost entirely emigrants.

The nature of the subsequent changes will depend upon the intensity of the inflammation, and upon the amount of liquid exuded into the serous cavity. If the inflammatory process subsides, and the liquid exuded is not sufficient to prevent the two surfaces of the membrane from coming into contact, they grow together and form an adhesion. This constitutes the so-called *adhesive inflammation*. The union is effected by the formation of connective tissue. The small round cells embedded in the fibrinous layer become elongated and spindle-shaped, numerous new bloodvessels are formed, and the fibrinous material fibrillates. Many of the vessels atrophy and disappear as the organization becomes complete. The process is thus precisely similar

to that which takes place in the union of an incised wound. It is probable also that in some cases union may take place without the intervention of any fibrinous layer, by the formation and growing together of irregular papillary outgrowths from the sub-endothelial tissue.

If, however, the inflammatory process is severe, or the surfaces of the membrane are separated by a large quantity of liquid effusion, organization and adhesion cannot be thus readily effected. If a large quantity of liquid exists in the serous cavity, the removal of this becomes necessary before union can take place. If the inflammatory process continues, or its intensity is great, union is prevented by the formation of pus. These two conditions must be considered separately.

The existence of a large amount of effusion prevents the adhesion of the serous surfaces, and before this can be effected the absorption of the liquid becomes necessary. The presence of the liquid itself, however, interferes with its absorption. This is owing, as already stated when speaking of the "Terminations of Inflammation," to the pressure which it exercises upon the bloodvessels and lymphatics, which pressure, by hindering the circulation in these vessels, tends not only to prevent absorption, but also to interfere with the restoration of the vascular walls to a normal state, and so to favor a continuance of the exudation. The removal of some of the liquid by artificial means consequently facilitates the absorption of the remainder. When the process is protracted, the sub-endothelial connective tissue becomes involved and infiltrated with small cells, and a richly vascular granulation-tissue is formed beneath the layer of proliferating endothelium. The endothelium itself becomes less abundant, and, if the inflammation subsides, the new granulation-tissue gradually develops into connective tissue, and thus a false membrane is formed, rich in vessels, which takes the place of the endothelial layer. As the liquid is absorbed, the two surfaces of the membrane come into contact and grow together, the new vessels becoming gradually obliterated.

If the inflammatory process does not subside, or from its commencement is of considerable intensity, it may be attended by the formation of large quantities of pus. In this case the emigration of blood-corpuscles is so considerable that the young elements exist in large enough numbers to give to the exuded liquids a purulent character. The condition is then termed *empyæma*. As the connective tissue becomes involved and a granulation-tissue is formed, this may continue to

generate pus like an ordinary granulating wound. If the pus be removed, the suppuration may gradually cease, the granulation-tissue develop into a fibrous structure, and the union of the serous surfaces thus be effected. The serous membrane becomes greatly thickened, and the new tissue undergoes considerable contraction in the process of its organization.

CHAPTER XLII.

INFLAMMATION OF THE LIVER.

INFLAMMATORY processes in the liver are either acute or chronic. *Acute* inflammations, leading to suppuration, are usually infective in their nature, resulting from the transmission of infective materials from lesions in the abdominal organs or in other parts. The processes are consequently most frequently disseminated and confined to small portions of the hepatic substance. The pus-corpuscles—which usually accumulate so as to form an abscess—are almost entirely emigrants, although recent investigations render it highly probable that they may originate by the endogenous proliferation of the liver-cells.

These suppurative inflammations are in the majority of cases pyæmic, and when pyæmic they are usually multiple. Hepatic abscess is also common in tropical climates, and here the abscess is commonly single. These tropical abscesses are sometimes associated with dysentery, and they may then probably result from the absorption of infective substances from the diseased intestine; but in other cases the abscess appears to be due to a primary inflammation of the hepatic tissue. As other causes of hepatic suppuration must be mentioned inflammation of the bile-ducts, such as sometimes results from gall-stones, etc.; and external violence.

Chronic inflammatory processes in the liver, being of much less intensity, lead to a gradual increase in the connective tissue of the organ, and consequently to induration and to the subsequent atrophy of its proper structure. They constitute what is known as *interstitial hepatitis*, or more commonly as *cirrhosis*.

Cirrhosis of the Liver.

Cirrhosis of the liver, or interstitial hepatitis, is characterized by a gradual increase in the connective tissue of the organ and by the subsequent atrophy of the liver-cells, so that when examined with a low magnifying power, the acini are seen to be separated by broad tracts of new interstitial growth. (Fig. 114.)

The process usually commences in the connective tissue surrounding the smaller branches of the portal vein, and gradually extends to that surrounding the larger ones, until ultimately the interlobular connective tissue throughout the whole organ may become involved. This tissue becomes infiltrated with small round cells, from which are produced a more or less completely fibrillated structure, containing in the earlier stages of its development numerous new bloodvessels, which are supplied by branches of the hepatic artery. The change is sometimes uniform, but more commonly it is much more advanced in some parts than in others. In many places the cellular infiltration may be considerable, whilst in others the fibrillation is much more marked; and if the process lasts long enough, the vascular and richly-cellular growth may gradually assume the characters of cicatricial tissue, the vessels at the same time becoming obliterated. (See Fig. 97.) In many cases this connective tissue growth is not limited to the interlobular tissue, but extends inwards so as to involve the inter-cellular network of the organ, which becomes much thickened and infiltrated with small cells. (Fig. 115.)

The effect of the new growth is ultimately to cause atrophy of the hepatic cells, and to obstruct the circulation through the portal capillaries and the passage of bile through the bile-ducts. This effect is materially increased by the process of contraction which the new tissue undergoes. The hepatic cells in the outer zone of the lobules are the first to atrophy. The cells become smaller, often undergo fatty metamorphosis, and ultimately are completely destroyed.

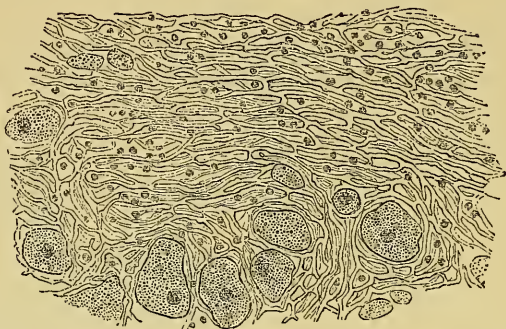
FIG. 114.



Cirrhosis of the Liver.—Showing the growth of connective tissue between the hepatic lobules. *a.* Lobules. *b.* New growth of interlobular connective tissue. $\times 16$.

(Fig. 115.) Those in the central parts of the lobule are in the earlier stages but little altered, although they are often stained with bile. As the growth extends, however, these also become annihilated, and the whole lobule may be replaced by connective tissue. The

FIG. 115.



Cirrhosis of the Liver.—A thin section from the external portion of one of the hepatic lobules.—Showing the new growth of connective tissue, and the way in which it involves the intercellular network and causes atrophy of the liver-cells. $\times 200$.

cells in the outer part of the lobules are sometimes infiltrated with fat prior to their destruction, the cirrhosis being associated with fatty infiltration. (See Fig. 8.)

In addition to the changes described, there is another condition often met with in cirrhosis—viz., a development of numerous biliary canaliculi in the portal canals. This is invariably present in that form of the disease which results from long-continued obstruction of the bile-ducts (Biliary Cirrhosis); but it appears not to be characteristic of this, being also sometimes met with in alcoholic cirrhosis, and in the cirrhosis of phthisis.¹

The physical characters of the cirrhotic liver vary. In the earlier stages of the disease the organ is probably always more or less increased in size; the enlargement being almost uniform, and the edge rounded and thickened. Later, atrophy and contraction take place, the liver diminishes and presents an irregular nodular surface. In other cases, however, the enlargement of the organ is considerable, there is but little subsequent atrophy, and the surface remains comparatively smooth up to the time of death (Hypertrophic Cirrhosis).

¹ See Paper on "Hypertrophic Cirrhosis of Liver," by Dr. Saundby: *Trans. Path. Soc. Lond.*, 1879, vol. xxx. p. 301.

Respecting the causes of these differences in the size of the liver, we are at present unable to speak certainly. In that form of cirrhosis which results from biliary obstruction, and which is characterized clinically by persistent jaundice and the absence of ascites, there is, as already stated, a considerable development of biliary canaliculi in the portal canals, and it is in this variety also that there is usually a marked infiltration of the intercellular tissue. These livers are commonly greatly enlarged and do not undergo subsequent contraction. The differences in the size of the liver in alcoholic cirrhosis probably depend in great measure upon differences in the age of the new growth, and in its distribution. In the large livers the growth is usually richly cellular and very generally distributed, often involving the intercellular tissue; whilst in the smaller atrophic forms of cirrhosis it is commonly more fibrous and less cellular in character, and its distribution is more partial. It is probable that in the larger livers the growth is in an earlier stage of development, and that if the patient had lived, the organ would have diminished in size. When the growth is irregularly distributed, it necessarily causes more irregularity in the configuration of the liver than when the distribution is more uniform. In some cases the large size of the organ is due to the cirrhosis being associated with fatty infiltration. (See Fig. 8.)

The cirrhotic liver is always increased in consistence. It breaks down less readily under the finger, and is often exceedingly firm and tough. On section, the new tissue is visible to the naked eye surrounding the lobules and in many parts completely replacing them. This gives to the cut-surface a mottled granular appearance, the lobules themselves contrasting with the new interlobular tissue; and this appearance is sometimes increased by fatty infiltration of the cells in the peripheral zone. The capsule also may be thickened, and the organ is frequently stained with bile.

The obliteration of the portal capillaries by the new tissue gives rise to ascites, hæmatemesis, diarrhœa, enlargement of the spleen, and to the other results of portal congestion. Obstruction of the bile-ducts, although it may cause staining of the hepatic substance, is rarely such as to interfere with the passage of the bile into the intestine, and hence there is usually but little general jaundice. In biliary cirrhosis jaundice results from the biliary obstruction which is the cause of the disease. The destruction of the liver-cells, by interfering with the glycogenic function of the organ, leads to marked interference with general nutrition.

Acute Yellow Atrophy.

This exceedingly rare disease of the liver is characterized by a rapid diminution in its size, and by destruction of the hepatic cells. The organ may, in the course of a few days, be reduced to less than half its natural bulk, being especially diminished in thickness. It is soft and flabby in consistence, bloodless, and of a dull yellow or yellowish-red color. The lobules are indistinguishable. When examined microscopically, the liver-cells are found to be completely destroyed, being replaced by granular débris, fat granules, and pigment. Tyrosin and leucin have been found in the disintegrated liver-tissue.

The pathology of this disease is exceedingly obscure. By some it has been regarded as an acute inflammatory process, by others as a passive-degeneration.

CHAPTER XLIII.

INFLAMMATION OF THE KIDNEY.

INFLAMMATORY processes in the kidney present certain variations according to their intensity. They comprise *suppurative*, *tubal*, and *interstitial* nephritis. Of these, suppurative nephritis, as the name implies, is an intense inflammation leading to the formation of abscess. This usually results from the transmission of infective materials from some primary lesions (pyæmic), or it is associated with some inflammatory condition of the lower urinary passages. Tubal nephritis is also an inflammation of considerable intensity, and in it the structural changes have their principal seat in the tubular epithelium. Interstitial nephritis is an inflammatory process which runs a more chronic course, and is of less intensity than either of the preceding. Consequently in it the principal structural changes take place in the connective tissue around the bloodvessels—in the intertubular connective tissue. (See “Chronic Inflammations.”) It must, however, be distinctly borne in mind that these two varieties of histological

changes—those in the tubular epithelium and those in the intertubular connective tissue—are very constantly associated. Tubal and interstitial nephritis cannot therefore be separated from one another by any distinct line of demarcation. They might, perhaps, be more correctly designated *acute* and *chronic* nephritis.

Suppurative Nephritis.

Acute inflammatory processes in the kidney attended by the formation of pus, give rise to *renal abscesses*. Such processes, as already stated, are often infective in their nature, resulting from the transmission of infective materials from some primary lesion, as in pyæmia; and they also occur in connection with inflammatory conditions of the urinary passages. In the latter they constitute what is commonly known as the “Surgical Kidney.”

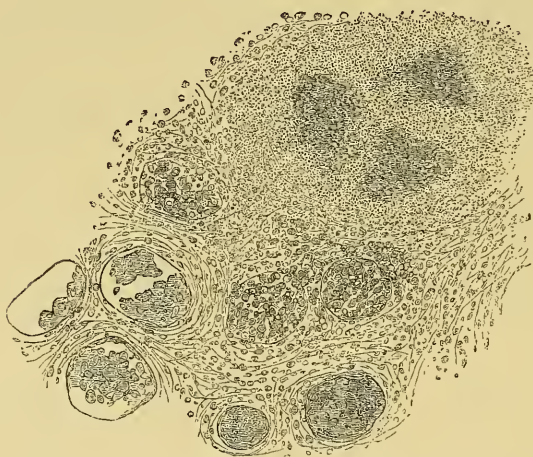
The abscesses met with in the kidney as the result of pyæmia are principally confined to the cortex, and they resemble pyæmic abscesses in other organs. They are usually multiple, and are often surrounded by a thin zone of red hyperæmic tissue. Their characters have been already described in the chapter on embolism. (See “Results of Embolism.”)

SURGICAL KIDNEY.—This is the name commonly given to those inflammatory conditions of the kidney which result from increased urinary pressure and inflammation of the lower urinary passages. These renal inflammations frequently occur in association with renal and vesical calculus, obstructed ureter, urethral stricture, enlargement of the prostate, etc. These, and other similar conditions, not only tend to impede the flow of urine and so to cause increased urinary pressure above the obstruction, but also, in most cases, to set up more or less inflammation of the lower urinary passages.

The changes which occur in the kidney vary. Simple long-continued increase of urinary pressure resulting from some obstruction to the flow of urine gives rise to chronic renal changes, which are characterized mainly by more or less cellular infiltration of the intertubular connective tissue. (“Interstitial Nephritis.”) This cellular infiltration, which is exceedingly irregular in its distribution, occurs both in the pyramids and cortex. The tubules are in some parts found blocked with epithelium, whilst in others they are wasted or obliterated. The walls of the small arteries are not thickened. Owing to these changes, the kidneys are somewhat enlarged, the capsule is slightly adherent,

the cut-surface paler than natural, and the consistence of the organs abnormally tough. As the process proceeds the pyramidal portions gradually become absorbed, the absorption commencing at the papillæ and extending until ultimately not only the pyramids but also the thickened cortex may disappear, and the kidney be converted into a large cyst. If, on the other hand, the urinary obstruction be removed, the processes of inflammation and absorption may cease, and the indurated kidney will then become contracted.

FIG. 116.



Surgical Kidney.—At the lower part of the figure is seen the cellular infiltration of the intertubular tissue, and the blocking of the tubes with epithelium and leucocytes. At the upper part, there is the commencing formation of an abscess. $\times 100$.

In other cases, and especially when the urinary obstruction is associated with inflammation of the lower urinary passages, the process is much more acute, the cellular infiltration of the intertubular tissue is much more abundant, and the young cells (emigrants) accumulate in certain situations in such numbers as to give rise to abscesses. (Fig. 116.) The blocking of the tubes with epithelium is then more marked, and many of them are found filled with the emigrant leucocytes. The kidney in such cases are usually not only enlarged and pale, but soft, although their consistence will depend upon the existence or not of the more chronic interstitial changes, and yellowish-white patches of various sizes are seen on their cut surface. Many of these patches have purulent centres, but they are not com-

monly surrounded by a zone of red hyperæmic tissue, as in pyæmia. Yellowish lines and striæ are also often seen extending from the papillæ to the bases of the pyramids. This acute suppurative process may occur independently of the more chronic lesions. Much more commonly, however, it supervenes in kidneys which have already undergone the more chronic and diffuse interstitial changes, and its supervention appears not unfrequently to be determined by the performance of some surgical operation in connection with the bladder or urethra.

Respecting the pathology of these changes in the kidney—they undoubtedly result from the inflammatory condition of the urinary passages, and the impediment to the escape of urine with which they are associated. As to the manner in which these conditions produce the kidney changes we are unable to speak certainly. The simple tension due to the urinary impediment is in itself sufficient to cause chronic interstitial changes. Respecting the more acute processes, Dr. Dickinson believes that in many cases these are due to the absorption of septic substances contained in the urine.¹ According to Mr. Marcus Beck, reflex irritation of the kidney caused by injuries of the bladder from calculus, operative interference, etc., is often an important causative element.²

Tubal Nephritis.

Tubal, parenchymatous, or acute nephritis, is that subacute inflammation of the kidney which constitutes the more acute form of Bright's disease—that form which is characterized by a more or less marked beginning, scanty and highly albuminous urine, and dropsy. In its more advanced stages it is the large kidney of chronic Bright's disease.

The changes which take place in the kidney have their seat mainly in the cortex. They comprise increased vascularity and exudation into the urine tubes, and swelling with, probably, proliferation of the tubular epithelium. The prominence of the vascular phenomena, however, varies very considerably in different cases.

¹ Dickinson on "Disseminated Suppuration of the Kidney:" *Med.-Chir. Trans.*, vol. lvi.

² Marcus Beck on "Nephritis and Pyelitis consecutive to Affections of the Lower Urinary Tract:" *Reynolds's System of Medicine*, vol. v.

In the most acute cases of Bright's disease—those which are induced suddenly from exposure to cold, the vascular changes are marked. In these cases the contraction of the cutaneous vessels and the check to the function of the skin caused by the chilling of the surface, lead to considerable hyperæmia of the organs. There is abundant exudation into the urine-tubes, many of the capillaries at the same time frequently rupture, and thus there is an escape of blood-corpuscles and of liquor sanguinis into the tubes of the cortex; hence the blood and “blood-casts” in the urine which are so characteristic of the early stages of the most acute forms of the disease. In this stage the process may quickly subside, and, with the exception of some swelling and desquamation of the tubular epithelium, no further alterations take place in the kidney.

In the less acute cases the vascular phenomena are less marked, and important changes take place in the tubular epithelium. The epithelial elements become swollen and granular. (Fig. 117.) The

FIG. 117.



Tubal Nephritis.—The earlier stage of the process. Showing the swelling of the tubular epithelium. In some of the tubes the epithelium has fallen out during the preparation of the section. $\times 200$.

granules, which are often so numerous as to occlude the nucleus of the cell, are soluble in acetic acid, and thus differ from molecular fat. This is the condition known as “cloudy swelling.” Many small cells are also seen within the tubes, and these have been supposed to be

the products of epithelial proliferation. It is probable that some of them are thus produced, although the majority must be regarded as having escaped from the vessels. Owing to these changes the tubes become distended with cellular elements. (Fig. 118.)

In addition to the cell-forms, many of the tubes also contain hyaline cylinders, which are commonly regarded as consisting of coagulated substances which have escaped from the vessels. By many pathologists, however, this hyaline material is supposed to be the product of a mucoid, or some allied, metamorphosis of the epithelium. The cell-forms contained within the tubes adhere to this hyaline substance, and some of them are washed away and appear in the urine as "epithelial casts." A varying number of emigrant leucocytes are also usually found around the Malpighian tufts.

The alterations which these changes produce in the physical characters of the kidneys vary according to the extent of the hyperæmia. The organs are always considerably increased in size, and more or less abnormally vascular. The capsule separates readily, exposing a perfectly smooth but vascular surface. The consistence is diminished, the tissue breaking with a soft, friable fracture. On section, the increase in the size of the organ is seen to be principally due to the increased thickness of the cortex. This is either of a reddish-brown, or of an opaque-white or pale buff color; these differences depending upon the relative proportion of blood and of accumulated intra-tubular elements. Although in the earliest stage of the most acute forms of the disease the color is redder than natural, it usually soon becomes pale and opaque. This is owing to the swelling of the epithelial elements and to the accumulation in the cortical tubes. The blood becomes expressed from the intertubular vessels, and hence the increased vascularity is most evident in the Malpighian corpuscles, beneath the capsule, and in the pyramidal portion of the organ. The Malpighian corpuscles stand out as prominent red points, and the pyramidal cones are of a deep red color, thus contrasting strongly with the pale opaque cortex.

The termination of the process varies. The increased vascularity and epithelial change may, as already stated, subside, and the in-

FIG. 118.

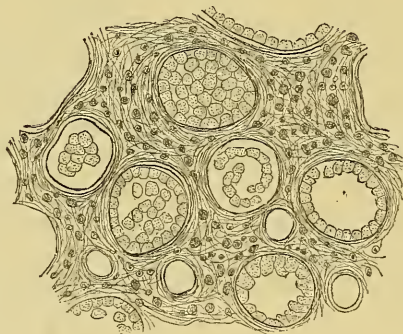


Tubal Nephritis. a Single Urine Tube.—Showing the accumulation within the tube. In the few epithelial cells which have escaped, is seen the granular condition of the protoplasm. $\times 200$.

flammatory products passing away in the urine, the organ gradually returns to its normal condition. In other cases the disease continues; and although the vascularity diminishes, the vitality of the epithelial elements become so much impaired that they undergo retrogressive changes. The cells then continue to come away with the urine, adherent to the casts, but instead of presenting the swelled granular appearance as in the earlier stage of the disease, they contain molecular fat. This fat gradually increases in amount as the degeneration proceeds, until ultimately the cells are destroyed, and it appears as free molecules and granules on the tube-casts.

This fatty degeneration of the epithelium is attended by corresponding changes in the appearance of the organ. The redness diminishes, and the Malpighian corpuscles are less prominent. The enlarged cortex presents a yellowish-white tinge, studded with minute yellowish streaks. This is owing to the presence of fat in the tubes of the cortex. This fatty stage, if only slightly advanced, may undoubtedly pass off. The degenerated cells are carried away by the urine, from those which remain in the tubes the fat is probably

FIG. 119.



Tubal Nephritis.—Duration of disease, six months. Kidneys large; capsules, non-adherent; surface, smooth; tissue, soft. Showing, in addition to the intratubular change, the cellular infiltration of the intertubular connective tissue. $\times 200$.

partially absorbed, the retrograde process gradually ceases, and the organ returns to nearly its normal size and condition. In other cases the degeneration continues, and, owing to the loss of epithelium, the kidney becomes somewhat diminished in size. This atrophy, however, I believe never occurs without changes in the intertubular connective tissue.

When the inflammatory process is of longer duration, or when the kidneys are the seats of repeated attacks of subacute inflammation, the intertubular connective tissue invariably becomes involved. This tissue becomes infiltrated with small cells which ultimately tend to form a fibrillated structure. (Fig. 119.) The new intertubular growth may gradually increase, and so lead to more or less irregular atrophy of the organ, such as will be described as occurring in interstitial nephritis. (See "Interstitial Nephritis.") In other cases death ensues before any marked atrophy has taken place, and thus the organ may remain smooth and large to the termination of the disease. The intertubular growth is sometimes found thickly studded with fatty granules.

SCARLATINAL NEPHRITIS.—The changes which take place in the kidney in scarlatina were formerly regarded as precisely similar to those which have been just described as tubal nephritis. Recent investigations, however, show that this view requires considerable modification. It has long been known that in scarlatina cases sometimes occur in which the kidney change differs from the type of ordinary acute nephritis; and such cases have been described by Prof. Klebs, as *glomerulo-nephritis*. It is mainly, however, owing to the more recent researches of Dr. Klein that any exact knowledge of the scarlatinal kidney exists.¹ The changes as described by Dr. Klein may be thus briefly summarized:—

The earliest changes—those occurring during the first week of the disease—comprise:—

1. Increase of the nuclei covering the glomeruli of the Malpighian corpuscles.

2. Hyaline degeneration of the elastic intima of minute arteries, especially of the afferent arterioles of the Malpighian corpuscles. This change produces a swelling of the intima, so as in some places to cause a distinct narrowing of the lumen of the vessel. The capillaries of the Malpighian corpuscles are in parts altered in the same way, in consequence of which many of them become impermeable.

These marked and early changes in the Malpighian corpuscles are important, as helping to explain those cases which are occasionally met with, in which death occurs from anuria and uræmia, and no catarrhal or other conspicuous alterations are found in the kidneys.

¹ "The Anatomical Changes of the Kidney and other Organs in Scarlatina of Man," by Dr. Klein: *Trans. Path. Soc. Lond.*, 1877, vol. xxviii.

3. Multiplication of the nuclei of the muscular coat of the minute arteries, and a corresponding increase in the thickness of the walls of these vessels.

4. Cloudy swelling of the epithelium in the convoluted tubes, with multiplication of the epithelial nuclei. Granular matter and even blood may also be found in the tubes, and in the cavity of Bowman's capsules. These parenchymatous changes are in the early stages of the disease but little marked.

The later changes—those occurring after the first week—consist in:—

5. A cellular infiltration of the intertubular connective tissue of the cortex (interstitial nephritis), together with an increase in the epithelial changes, and a crowding of the tubes with small round cells (leucocytes). The cellular infiltration commences around the larger vascular trunks, whence it spreads rapidly into the bases of the pyramids, and especially into the cortex. As it increases the epithelium undergoes fatty degeneration, and the urine-tubes gradually become obliterated.

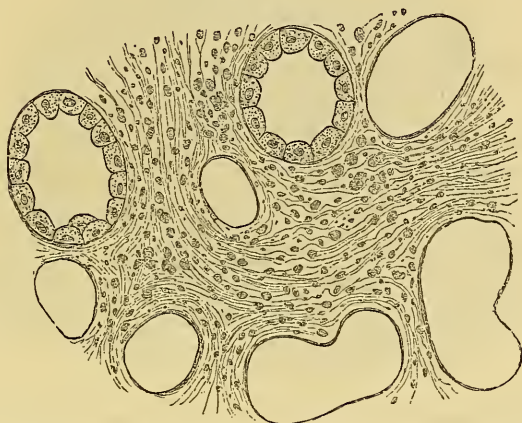
Interstitial Nephritis.

Interstitial or chronic nephritis is characterized by a gradual increase of the connective tissue of the kidney and by atrophy of the tubular structures. This, as has been seen, often occurs in the more advanced stages of tubal nephritis (see Fig. 119); in scarlatinal nephritis; and also as a result of obstruction in the lower urinary passages. It is, however, most frequent, and constitutes the most prominent structural change in that variety of Bright's disease which is known as chronic Bright's disease with contracted kidney, and which is characterized clinically by insidious onset, increased secretion of urine, with the absence both of albuminuria and of dropsy.

The changes in the kidneys in this most chronic form of Bright's disease are usually exceedingly gradual in their onset, and are not preceded by any marked vascular phenomena or by any activity in the tubular epithelium. The first change appears to consist in some cellular infiltration of the intertubular connective tissue. (Fig. 120.) Usually, however, the cells are not numerous, and the new tissue is more or less developed into a fibrillated structure. This is the condition in which it is commonly met with. These changes are almost entirely limited to the cortical portion of the kidney, and although here they are more or less general, the new growth is more abundant

in some parts than in others, being usually most so around the Malpighian bodies and in the neighborhood of the capsule, with which it is closely united. In this stage the tubes and their epithelium are unaffected.

FIG. 120.



Interstitial Nephritis.—The earlier stage of the process. Showing the cellular infiltration of the intertubular connective tissue. The epithelium has fallen out of some of the tubes during the preparation of the section. $\times 200$.

In this early stage, the kidney may be somewhat increased in size, the capsule usually separates less readily than in health, and the surface of the organ is slightly granular. On section, the cortical substance is in some cases paler, in others redder than natural. The cut-surface also looks obscurely granular. The Malpighian bodies stand out as red points, and the bases of the pyramids and surface of the organ are sometimes hyperæmic. The consistence of the kidney is usually slightly denser and tougher than natural. This, however, will vary with the character of the new growth, as will also the increase in size and the irregularity of the surface. If the new tissue is slowly developed, the size will be but little increased, whereas the increase in consistence and the granular condition will be more marked. If, on the other hand, the process be more rapid, and the cellular infiltration more abundant, there will be a greater increase in the size, the granular character will be slight, and the consistence may be even softer than natural.

The second stage in the process is characterized by the atrophy of the tubular structures. This is probably mainly owing to the pressure exercised by the intertubular growth, and to the cicatricial

contraction which it often undergoes. The atrophy consequently is not uniform, but is more marked in some parts than in others. The

FIG. 121.



Interstitial Nephritis.—An advanced stage of the process. Showing the intertubular tissue with the granular and fatty débris which result from degeneration. $\times 100$

tubes are now found in many parts diminished in size, or completely obliterated; whilst in others they are irregularly dilated, and filled

FIG. 122.



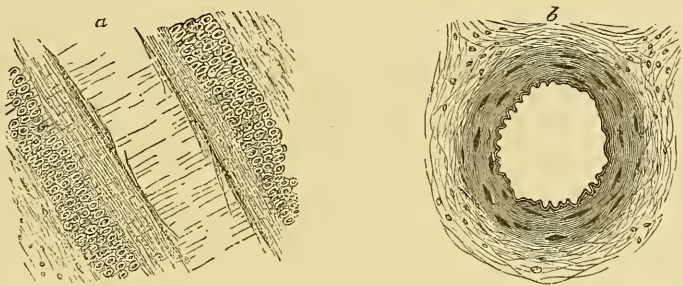
Interstitial Nephritis.—A very advanced stage in the process. Showing the large amount of tissue between the tubes of the cortex, and the extensive atrophy of the tubes. The degenerated epithelium which was contained in some of the tubes has fallen out in the preparation of this section. $\times 50$.

with degenerated epithelial products. Their walls are usually thickened. As the atrophy proceeds the intertubular tissue thus becomes

mingled with the granular and fatty débris which results from the retrograde process. (Fig. 121.) The Malpighian bodies become approximated, and the secreting structure throughout large tracts of the kidney is destroyed. (Fig. 122.) The irregular pressure exercised by the new growth also gives rise to the formation of cysts. These originate partly in the Malpighian capsules, and partly in the urine tubes—the latter becoming irregularly dilated.

The small arteries of the kidney also undergo important alterations. These were first described by Dr. Johnson. Dr. Johnson states that the walls of these vessels are thickened, owing to hypertrophy of their longitudinal and circular muscular fibres. This change is well represented in the accompanying drawing. (Fig. 123.) Both the internal longitudinal and the external circular muscular fibres are considerably increased. The external fibrous coat of the vessel is also thickened, and it appears to be continuous with the new intertubular tissue. This thickening of the external coat has been especially insisted upon by Sir W. Gull and Dr. Sutton. I have usually found it associated with the muscular hypertrophy, which is undoubtedly the most prominent structural change.

FIG. 123.



Arteries from contracted Kidney of advanced Chronic Bright's Disease.—*a.* Longitudinal section, showing the great thickening of the internal longitudinal and external circular muscular coat, also of the outer fibrous coat. *b.* Transverse section of another vessel less diseased. Here is seen the thickening of the circular muscular and external fibrous coat. $\times 200$.

In this more advanced stage of the disease the kidney is diminished in size. Its surface is more granular, the capsule more thickened and adherent, and it cannot be removed without tearing the kidney substance. The superficial vessels are seen unduly marked in the depressions between the granulations. The cortex is tough and fibrous, of a

reddish, yellowish-gray or buff color, mottled with yellow streaks and patches; and usually numerous small cysts are distributed throughout it. Calcareous deposits are also sometimes seen as white streaks between the tubes of the pyramids.

CHAPTER XLIV.

INFLAMMATION OF THE BRAIN AND SPINAL CORD.

INFLAMMATORY processes in the nervous centres are probably much less frequent than was formerly supposed. Many of those morbid changes in the brain and spinal cord which are attended by softening, and which were at one time regarded as the result of inflammation, are now known to owe their origin to simple interference with the vascular supply, such as results from thrombosis, embolism, or degenerative changes in the walls of the bloodvessels. (See "Cerebral Softening.")

The injury which determines the occurrence of intense inflammations in the brain or cord is most frequently some external violence—a blow, simple concussion, or fracture of the osseous framework. In other cases it is diseased bone, as in the inflammation of the brain which so often results from disease of the petrous portion of the temporal bone. Lastly, in a comparatively few number of cases these inflammations are pyæmic.

The inflammatory process is almost invariably limited to small portions of the cerebral or spinal substance. The earliest change consists in a more or less intense and localized hyperæmia, which is frequently attended by rupture and minute extravasations of blood. The nervous tissue then becomes infiltrated with young cells and considerably softened, and it presents a uniform red or mottled color. This red softened tissue gradually acquires a brownish or brownish-yellow color owing to changes in the hæmoglobin. The nerve-fibres, nerve-cells, and cells of the neuroglia then become disintegrated and often undergo more or less fatty degeneration; and thus the so-called "inflammatory" or "exudation corpuscles" are frequently met with. (See Fig. 15.)

In many cases the accumulation of young cells is sufficient to give rise to the formation of an abscess, and a yellowish or reddish purulent liquid gradually takes the place of the original softened mass. The tissue surrounding the abscess is also hyperæmic, softened, and infiltrated with cells. The cellular infiltration may gradually extend, and thus the abscess increase in size until it opens either externally or into the ventricles. In other cases the abscess becomes limited and encapsuled by the formation of connective tissue from the neuroglia, and this tissue often forms a delicate network traversing the cavity. When the products of these intense inflammations have thus become encapsuled they may gradually dry up into caseous or calcareous masses, or the absorption may be more complete, so as to leave little more than a cicatrix. Respecting the source from which the young cells are derived—they are probably entirely emigrants. The nerve-cells themselves, and the cells of the neuroglia, appear to undergo no active changes in inflammation.

Suppurative inflammations are much more common in the brain than in the spinal cord. In the latter the inflammatory process is rarely of sufficient intensity to produce abscess; it causes merely softening of the nervous tissue, and, when not secondary to a meningitis, usually involves primarily and principally the central gray matter (myelitis).

INFLAMMATORY SOFTENING OF THE BRAIN AND CORD.—Conditions of softening of the cerebral or spinal substance resulting from inflammation, other than those which have been above described, probably rarely occur as *primary* lesions. Most varieties of softening which were formerly described as inflammatory—either from the red color of the softened tissue or from the acuteness of the process—result, as already stated, from vascular obstruction; either from the more sudden occlusion of the vessels by an embolus or thrombus, or from the more gradual obstruction due to atheromatous, calcareous, or syphilitic disease of the vascular walls. (See “Cerebral Softening.”) Inflammation and consequent softening of the nervous tissue, however, sometimes occurs as a *secondary* process. It takes place especially around clots of blood or other morbid products within the brain or spinal cord, and results from the injurious influence which these substances exercise upon the immediately adjacent structures. Such a result is not unfrequent in cases of cerebral hemorrhage. The nerve-tissue immediately surrounding the clot becomes the seat of an inflammatory process, and it is found after death softened, hyperæmic,

and infiltrated with young cells. Inflammation of the superficial portions of the cerebral and spinal substance may also occur as the result of meningitis.

Sclerosis of the Brain and Spinal Cord.

The term "sclerosis" is applied to certain changes in the nervous centres which are characterized by an increase of the connective tissue (neuroglia), and by atrophy and degeneration of the proper nervous elements. The affected portions are, for the most part, increased in consistence; sometimes, however, they are softer than natural. They usually present a somewhat translucent appearance, and are of a grayish-color; hence the change has been called "gray degeneration." The gray color appears to depend upon the loss of the white substance of the nerve-fibres. The altered tissue also stains deeply with carmine. This is owing to the fact that the white substance of the nerve-fibres does not stain, but the connective tissue stains deeply. Hence the degree of staining is valuable as indicating, even to the naked eye, the degree of the sclerosis.

When the diseased portions of the brain and cord are examined microscopically, the cut ends of the nerve-fibres are seen, in transverse sections, to be separated by a granular, finely nucleated, and often partially fibrillated tissue, which evidently originates from the neuroglia. (Fig. 124.) The nerve-fibres themselves are atrophied, as are also the nerve-cells when the gray matter is involved; and in advanced stages of the process but few axis-cylinders or nerve-cells may be visible. In many cases the nucleated character of the interstitial growth is wanting. The walls of the blood-vessels are also stated to be thickened, and their nuclei to be increased.

FIG. 124.



Sclerosis of Spinal Cord.—From a case of progressive Muscular Atrophy. A transverse section. Showing the atrophy and disappearance of the nerve-fibres, and the new tissue between them. $\times 200$.

Sclerosis is more common in the spinal cord than in the brain. In the latter it occurs most frequently in small patches limited to certain portions of the brain. These must be distinguished from the cicatrices left after the absorption of blood or of inflammatory products. Sclerosis of the cord may in the same way be localized and more or less disseminated; more commonly,

however, it implicates only particular nervous tracts. It occurs thus in the posterior columns of the cord in locomotor ataxy, in the anterior cornua in progressive muscular atrophy, and in the pyramidal tracts as the result of destroying lesions in the motor tract above ("Secondary Degeneration"). In the localized and disseminated forms of sclerosis the cellular character of the new growth is usually more marked than it is in the simple uniform sclerosis which involves particular nerve tracts.

Respecting the nature of the change—it is probably in many cases the result of a chronic inflammatory process, the new growth of connective tissue leading to the destruction of the nerve elements. In other cases, however, the atrophy of the nerve tissue appears to precede the interstitial increase, so that the process would rather be regarded as a passive degeneration. This is probably the case in the secondary degenerations of the cord.

CHAPTER XLV.

INFLAMMATION OF THE LUNGS.

IN the lungs inflammatory processes comprise the three following principal varieties: *Croupous*, *broncho-* or *catarrhal*, and *chronic* or *interstitial* pneumonia. Of these, the former occurs as an independent affection, whereas the two latter are usually the result of some antecedent bronchial or pulmonary inflammation.

Croupous Pneumonia.

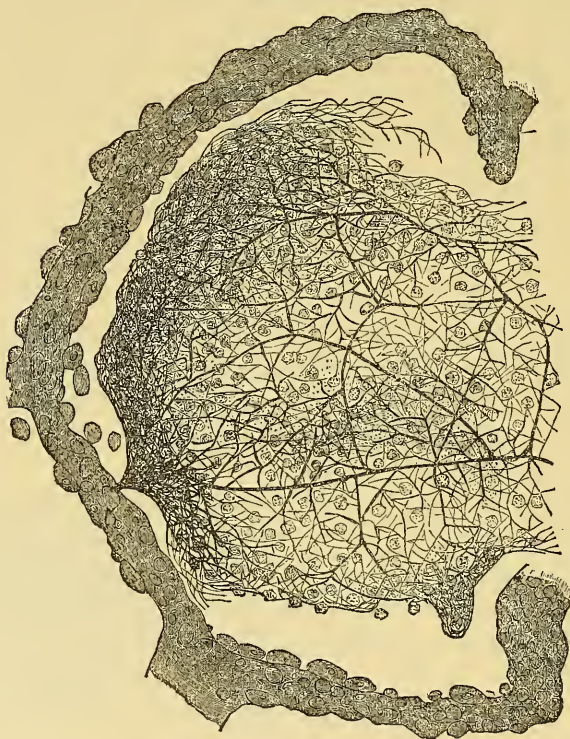
Croupous exudative, or *lobar* pneumonia, is that form of pulmonary inflammation which is met with in the disease known as acute primary pneumonia. This is now regarded as a *general* disease of which the pneumonic consolidation is the prominent local lesion.

The local process is characterized by intense inflammatory hyperæmia of the lung, and by the exudation of a large amount of coagulable material into the pulmonary tissue. It is termed "croupous" by the

Germans, from the supposed resemblance of the histological process to that of croup. The term “lobar” is applied to it because it almost invariably affects an extensive portion of the lung. The process is commonly described as consisting of three stages—1st, that of *engorgement*; 2d, that of *red hepatization*; and 3d, that of *gray hepatization*.

In the *first* stage, that of *engorgement*, the lung becomes exceedingly vascular, the changes in the bloodvessels and circulation being such as have been already described as characteristic of inflammation. The

FIG. 125.



Croupous Pneumonia—Red Hepatization.—Showing the fibrinous coagulum in one of the pulmonary alveoli, inclosing within its meshes numerous leucocytes, which are already commencing to undergo fatty metamorphosis. A few leucocytes are also seen on the alveolar walls, and the alveolar epithelium is swollen and granular. $\times 200$.

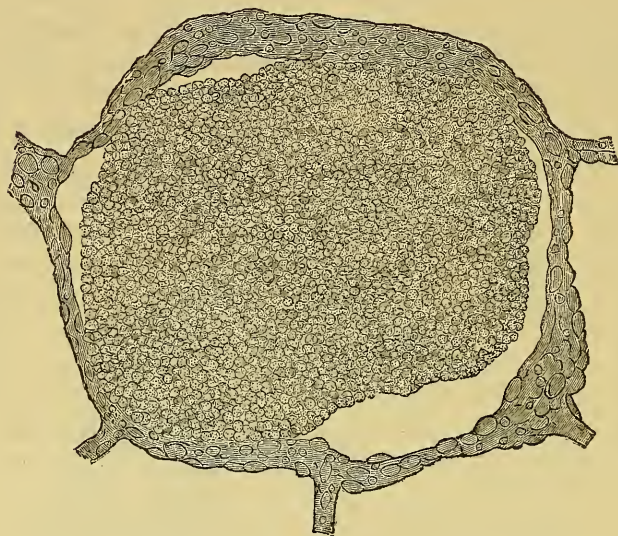
organ is of a dark red color, its specific gravity and absolute weight are increased, its elasticity is diminished, it is less crepitant and more friable than natural, and pits upon pressure. Its cut surface yields a reddish, frothy, tenacious liquid.

In the *second* stage, that of *red hepatization*, there is an exudation of liquor sanguinis and migration of blood-corpuscles into the pulmonary tissue. Some of the vessels may also rupture, and thus small extravasations occur. The exuded liquids coagulate within the air-vesicles and terminal bronchioles, the coagulum inclosing numerous white and some red blood-corpuscles. (Fig. 125.) It is stated by some German pathologists that the coagulum is in part produced by certain changes in the epithelium like those believed to occur in croup. (See "Croupous Inflammation of Mucous Membranes.") The lung is now much heavier than in the preceding stage, and is increased in size, so as to be often marked by the ribs. It is quite solid, sinks in water, and cannot be artificially inflated. It does not crepitate under the fingers, but is remarkably friable, breaking down readily with a soft granular fracture. The cut surface has a markedly granular appearance, seen especially when the tissue is torn. This is owing to the plugs of coagulated exudation matter which fill the alveoli. The color is of a dark reddish-brown, often here and there passing into a gray. This admixture with gray sometimes gives a marbled appearance. Throughout this stage there appears to be but little alteration either in the alveolar walls or in the alveolar epithelium. On the former are often seen a few leucocytes, and the latter is usually swollen and granular. (Fig. 125.) The pleura covering the solid lung always participates more or less in the inflammatory process. It is opaque, hyperæmic, and coated with lymph.

The *third* stage, that of *gray hepatization*, is characterized by a continuance in the emigration of leucocytes, and by cell-proliferation. The white blood-corpuscles continue to escape from the vessels, and thus their number within the alveoli gradually increases. The epithelial cells lining the alveolar walls, which were only swollen and granular in the earlier stage of the process, now undergo more active changes. Their nuclei enlarge and multiply, and ultimately numerous new cells are produced. The pulmonary alveoli thus become completely filled with young cell-forms, so that the fibrinous exudation is no longer visible as an independent material, as it is in the stage of red hepatization. (See Fig. 125.) The fibrinous material now disintegrates, and the young cells rapidly undergo retrogressive fatty changes, so that, as usually seen, the alveoli are filled with granular elements, which in many parts have lost their distinctive outlines. (Fig. 126.) The alveolar walls themselves, with few exceptions, remain throughout the process unaltered, although occasionally when this stage is

unusually advanced they may be found, here and there, partially destroyed. The weight, density, and friability of the lung now become even greater than in the stage of red hepatization, although the granular aspect of the cut surface is much less marked. The tissue is now

FIG. 126.



Croupous Pneumonia—Gray Hepatization.—Showing the large accumulation of cellular elements within one of the pulmonary alveoli, which in some parts have undergone such excessive fatty degeneration that their distinctive outlines are no longer visible. $\times 200$.

quite soft and pulpy, and a puriform liquid exudes from its cut surface. The most prominent feature, however, is the alteration which takes place in the color of the organ. This gradually changes from a dark reddish-brown to a gray or yellowish-white. This is owing partly to the pressure exercised upon the bloodvessels by the exuded substances and newly formed cells, and partly to the fatty degeneration which the latter have undergone. The stage of gray hepatization when far advanced has been termed suppuration of the lung.

Although these three stages of the pneumonic process have been described as succeeding one another in orderly succession, it must be remembered that each stage does not occur simultaneously throughout the whole of the affected area of the lung. The changes advance irregularly, so that whilst one portion of the lung is in the stage of red hepatization, another may be in the gray stage—hence the mottled marbled appearance of the consolidation. The rapidity with which the several stages succeed one another is also subject to marked vari-

ations. In some cases the pneumonic consolidation very rapidly becomes gray, whilst in others the time occupied in the transition is much longer.

The pneumonic process may terminate in the four following ways:—

1st. *In Resolution*.—The gradual return of the lung to its normal condition is the natural and much the most frequent termination of croupous pneumonia. This is effected by the fatty and mucoid degeneration of the inflammatory products which have accumulated within the alveoli, which thus become so altered that they can be removed by absorption. Granular pigment is also mixed with the softened matters and appears in the expectoration. This is probably partly derived from the extravasated blood, and is partly that which normally exists in the interlobular connective tissue. Where this process of liquefaction and disintegration is taking place in the lung the granular appearance of its cut surface is completely lost. It is of a yellowish-gray color, and a tenaceous puriform liquid can be expressed from its substance. As the softened matters become absorbed, the circulation is gradually restored and the organ ultimately attains its normal characters.

2d. *In Abscess*.—The formation of abscess is a rare result of simple pneumonia. Such a result appears to be favored by a bad constitution, and by any circumstances which tend to impair the general health, especially the abuse of alcohol. The abscess is more common in the upper than in the lower lobes. Circumscribed gangrene of the lung may also occasionally terminate in abscess. This takes place by the evacuation of the necrotic tissue through the bronchi, and the formation of a pyogenic membrane from the walls of the cavity, which generates pus. The cavity may ultimately close by granulation and cicatrization. These abscesses of primary origin are usually single, and thus differ from those due to pyæmia.

3d. *In Gangrene*.—This, which is also rare, is most common in chronic drunkards and in those of debilitated constitution. Two conditions appear to be principally concerned in bringing about this result: one is the interference with the supply of blood by the extensive formation of coagula in the pulmonary and bronchial vessels, together with considerable hemorrhage into the pulmonary tissue; the other is the injurious influence of septic inflammatory products. The gangrene is usually limited to a small area of the pneumonic lung, and is either diffuse or limited by a zone of inflamed tissue.

4th. *In Chronic Pneumonia*.—If the inflammatory process does not subside and the exuded substances are not absorbed, the alveolar walls gradually become involved. These become thickened by a new growth of fibro-nucleated tissue, and thus is produced more or less fibroid of induration of the organ. (See “*Interstitial Pneumonia*.”) This termination of croupous pneumonia is comparatively rare.

A croupous pneumonia plays a prominent part in some cases of pulmonary phthisis. (See “*Pulmonary Phthisis*.”)

Broncho- or Catarrhal Pneumonia.

Broncho-, catarrhal, or lobular pneumonia is inflammation of the lung-tissue associated with, and usually secondary to, inflammation of the bronchial mucous membrane. In the earlier stage, the pulmonary inflammation is commonly limited to scattered groups of air-vesicles, hence the term *lobular* which is applied to it. As the process proceeds, the inflammatory nodules may gradually coalesce, so as to produce larger tracts of consolidation. The inflammatory products which fill the alveoli, consist largely of cells derived from the epithelium of the alveoli and from the bronchial mucous membrane; exudation and emigration play a much less prominent part in the process than they do in croupous pneumonia. Owing to this preponderance of epithelial products, and to the association of the pulmonary with the bronchial inflammation, the process has been termed *catarrhal pneumonia*.

PATHOLOGY.—The pneumonic process, as already stated, is invariably associated with bronchial catarrh. In some cases, it would appear that the injury which produces the bronchial inflammation produces at the same time inflammation of the air-vesicles, but much more frequently the bronchitis precedes the pneumonia, and gives rise to it in a manner to be hereafter described. Whatever causes inflammation of the bronchial mucous membrane may thus be a cause of broncho-pneumonia. Simple bronchitis, especially in childhood and old age, and also the specific bronchitis associated with measles and whooping-cough, are the most frequent precursors of the disease. All conditions which tend to impair the general health favor the occurrence of the pneumonia. They do so by rendering the bronchial mucous membrane abnormally liable to become inflamed, and also by diminishing the power of the respiratory muscles, and thus aiding in the production of pulmonary collapse.

Inflammation of the bronchial mucous membrane may give rise to broncho-pneumonia in two ways: 1st, by causing in the first place

collapse of the lung-tissue; and 2d, by the direct extension of the inflammation from the bronchi to the air-vesicles. Of these the former is much the most frequent. The pneumonic process being the result of the bronchitis, almost invariably involves both lungs.

1. *Broncho-pneumonia consecutive to Collapse*.—Collapse of the lung-tissue greatly favors the occurrence of broncho-pneumonia, and usually the pneumonic process is principally confined to those portions of the lung in which collapse has taken place. There are two circumstances principally concerned in the production of the collapse which is consecutive to bronchitis—the narrowing or occlusion of the bronchial tubes due to the inflammatory swelling of the mucous membrane and the catarrhal secretion, and the weakness of the inspiratory power. The collapse thus induced is especially frequent in the posterior and inferior portions of the lungs—those portions in which normally the inflation of the lung is least complete. Commencing here, the process may gradually extend upwards till large areas of the lungs become involved. In other cases, owing to a more irregular distribution of the bronchial obstruction, the collapse is limited to small isolated portions of the lung. These portions vary in size from a hemp-seed to a walnut. They are commonly more or less wedge-shaped, with their apices towards the bronchus with which they communicate, and the lung-tissue around them usually presents various degrees of congestion and emphysema.

The tendency of the pneumonic process to occur in the collapsed portions of the lung is due partly to the hyperæmia which is induced by the collapse, and partly to the irritation of inhaled bronchial secretion. Collapse of the lung-tissue invariably induces more or less congestion. This is owing to the absence of the expansion and contraction of the air-vesicles which normally aid the pulmonary circulation, and also to the impediment to the blood-flow resulting from imperfect aëration. This congestion is quickly followed by œdema, and the bluish-purple collapsed portions of the lung become darker in color, less resistant, and more friable in consistence. In lung thus altered, a quasi-inflammatory process characterized mainly by epithelial activity is prone to supervene.

Another circumstance which often appears to play a prominent part in the causation of the pneumonic process is the presence within the alveoli of the inflammatory products of the bronchial mucous membrane. These products are frequently found in scattered groups of air-vesicles, and they are evidently inhaled. (See Fig. 127.) They

are found both in the air-containing and in the collapsed portions of the lung, but especially in the latter, the presence of collapse necessarily interfering with their removal by expectoration or absorption. These inhaled products are often found filling small groups of alveoli *without any evidence of subsequent inflammation*, and there can be no doubt that many of the patches of consolidation which are usually described as pneumonic are really non-inflammatory in their nature, and are thus produced. At the same time, owing to the irritation of the inhaled secretion, it tends to induce inflammatory changes within the alveoli, and these changes are frequently largely owing to its presence.

2. *Broncho-pneumonia independent of Collapse*.—Although the pneumonic process is usually consecutive to collapse, it may occur independently. This may be owing either to the direct extension of the inflammation from the bronchi to the air-vesicles, or to the influence of inhaled inflammatory products. In other cases, it is possible that the injury which causes the bronchitis causes at the same time inflammation of the pulmonary alveoli.

HISTOLOGY, ETC.—The appearances presented by the lungs after death vary. The bronchi are always more or less inflamed, and contain thick mucus. The lung-tissue exhibits, associated in various degrees, collapse, congestion, œdema, emphysema, and pneumonic consolidation. The bluish, non-crepitant, depressed portions of collapse, which become darker and more friable with age, are usually most abundant in the lower lobes and margins of the lungs. The collapse sometimes involves the whole of one lobe, but more commonly it is limited to smaller areas. When scattered and limited in its distribution, there is usually more or less emphysema of the intervening portions of the lung.

Those portions of the lungs in which the pneumonic process has supervened most commonly appear as scattered nodules of consolidation, varying in size from a small pea to a hazel-nut. These are ill-defined, and pass insensibly into the surrounding tissue, which is variously altered by congestion, collapse, and emphysema. They are of a reddish-gray color, slightly elevated, smooth, or very faintly granular, and soft and friable in consistence. As they increase in size they may become confluent. In a more advanced stage, the nodular and more diffuse consolidation becomes paler, firmer, drier, and somewhat resembles in appearance ordinary gray hepatization.

When examined microscopically, this consolidation is seen to consist of an accumulation within the alveoli of a gelatinous mucoid-looking

substance, small cells resembling leucocytes, and epithelial elements. In many cases much of this accumulation is precisely similar to that contained in the smaller bronchi, and it is evidently the inflammatory and richly cellular bronchial secretion which has been inhaled. (Fig. 127.) It is also often partly the result of exudation and emi-

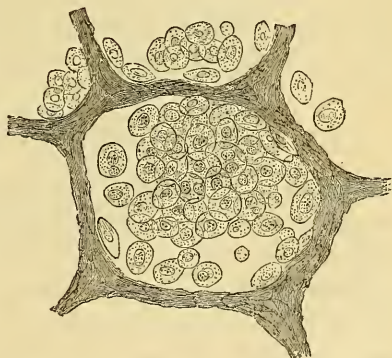
FIG. 127.



Broncho-Pneumonia.—From a child, aged four, with capillary bronchitis. A section of one of the patches of consolidation. Showing the stuffing of the alveoli with what appears in the main to be inhaled bronchial secretion. $\times 200$.

gration from the pulmonary capillaries; for, as shown by Cohnheim, blood-stasis so injures the walls of the bloodvessels that the blood-corpuscles and liquor sanguinis readily permeate them. (See “Inflammation.”) Associated with this material are large epithelial elements, the offspring of the alveolar epithelium. These vary considerably in number. In some cases, and in some portions of the consolidation, they may be very few, whilst in others they may constitute the predominant change. (Fig. 128.) These differences probably depend upon how far the inhalation of bronchial secretion constitutes a part of the process.

FIG. 128.



Catarrhal Pneumonia.—From a case of acute phthisis. Showing the large epithelial cells which fill the alveoli. $\times 200$.

The subsequent changes which take place in the lungs vary. When the disease does not end in death, resolution is the most common termination. The contents of the alveoli

undergo fatty metamorphosis, and are removed by expectoration and absorption, the lung gradually regaining its normal character. This process, however, is less readily effected than in croupous pneumonia, and it often occupies such a lengthened period that some thickening of the bronchial and alveolar walls and dilatation of the smaller bronchi remains. In chronic cases this fibroid thickening is much more marked, and considerable irregularly distributed pigmented induration and bronchial dilatation may be produced. (See "Chronic Pneumonia.") In these chronic forms the contents of the alveoli sometimes caseate, and then become encapsuled, or in quite exceptional cases lead to disintegration.

HYPOSTATIC PNEUMONIA.—Allusion must be made here to a form of lung-consolidation which is often described as pneumonic, but which, in reality, is for the most part non-inflammatory in its nature. This is the so-called hypostatic pneumonia. This condition is met with at the bases and most dependent portions of the lungs in the course of both chronic and acute diseases, and also in the aged and debilitated. It consists in the main of collapse, hyperæmia, and œdema of the lung-tissue, resulting from weak inspiratory power, feeble circulation, and gravitation. The consolidation thus mechanically induced is increased by more or less exudation of liquor sanguinis and blood-corpuscles into the alveoli, which exudation is partly due to the damage to the walls of the capillaries caused by the blood stasis. This condition of hypostasis is, as has been already stated, especially favorable to proliferation of the alveolar epithelium; and this proliferation often occurs to a greater or less extent, and so tends to increase the consolidation.

Interstitial or Chronic Pneumonia.

Interstitial or chronic pneumonia is characterized by a gradual increase in the connective tissue of the lung, which leads to an induration of the pulmonary texture, and to progressive obliteration of the alveolar cavities. It is commonly associated with catarrh and dilatation of the bronchi, and often with ulceration of the bronchial walls, and excavation of the indurated lung.

PATHOLOGY.—It is exceedingly doubtful if interstitial pneumonia is ever a primary and independent affection. It probably in all cases owes its origin to some antecedent inflammation of the pulmonary or bronchial textures, or of the pleura. It may be stated generally

that all inflammatory processes in the lungs which become chronic lead to an increase of the connective-tissue elements, and consequently to a fibroid induration of the organs, and in this respect, therefore, these processes resemble similar ones in other parts—*e. g.*, in the liver, kidney, and mucous membranes. In the lungs, by far the most common cause of such induration is phthisis, in all cases of which, excepting in those which are the most acute, there is more or less fibroid growth. The most chronic cases of phthisis—those in which the fibrosis is the most marked—are, it must be admitted, somewhat closely allied to some forms of interstitial pneumonia. The two diseases differ, however, in this respect: that whereas much of the pulmonary consolidation of phthisis tends to undergo molecular death and disintegration, that of interstitial pneumonia exhibits no such tendency, but any destruction and excavation of the indurated lung which may take place is due to secondary inflammation and ulceration commencing in the bronchial walls. In considering the pathology of interstitial pneumonia, therefore, it is necessary to exclude, in the first place, the pulmonary fibrosis of chronic phthisis. (See “Pulmonary Phthisis.”) Interstitial pneumonia must also be separated from that

FIG. 129.



Chronic Bronchitis.—Showing the new growth of fibro-nucleated tissue around the bronchus *b*, and the way in which this tissue is invading the walls of the adjacent alveoli. *v*, A divided bloodvessel. $\times 100$, reduced $\frac{1}{2}$.

form of pulmonary induration which is produced by long-continued mechanical congestion (see “Brown Induration of the Lung”), and from those more localized indurations due to chronic bronchitis (Fig. 129), and to syphilis.

There appear to be four conditions which may give rise to interstitial pneumonia. These are as follows:—

1. *Croupous Pneumonia*.—The pulmonary consolidation of acute croupous pneumonia in almost all cases undergoes complete resolution. This resolution is usually effected rapidly, but occasionally it is more protracted. When protracted, the hepatized lung tends to become slightly indurated, owing mainly to thickening of the walls of the alveoli. This indurated hepatization differs but little in its physical characters from ordinary red and gray hepatization; it is simply somewhat firmer, more resistant, and less granular. In very exceptional cases this small amount of induration, commencing in the alveolar walls, may gradually increase, so as ultimately to give rise to that extensive fibrosis of the lung which constitutes what is usually known as interstitial pneumonia.

2. *Broncho-Pneumonia*.—This appears to be a somewhat more frequent cause than the preceding. The greater liability of this form of pneumonia to lead to pulmonary induration is to be accounted for, partly by its longer duration and greater tendency to become chronic, and partly by the existence of bronchial dilatation with which it is so frequently associated. That bronchial dilatation is favorable to an indurative pneumonic process has been insisted upon by Dr. Wilson Fox.¹ The existence of this dilatation favors the persistence of the catarrhal and pneumonic process. The removal of secretion is rendered difficult, and the retained secretion tends to keep up and increase the irritative process both in the dilated bronchi and also in the pulmonary alveoli, and this persistence of the bronchial and pulmonary inflammation leads to fibroid thickening of the bronchial and alveolar walls. In this way areas of fibroid induration are produced, which, as the process proceeds, may ultimately involve large portions of the lung. The progressive tendency of the process is probably partly to be explained by the fact that pulmonary fibrosis is a cause of bronchial dilatation, so that fibrosis once established, by inducing further dilatation of the bronchi favors the extension of the bronchial and pulmonary induration (Wilson Fox).

Under this head may also be included those cases of induration and ulceration of the lung which result from obstruction of a main bronchus—such as is produced by the pressure of an aneurism. Here the retained bronchial secretion sets up inflammatory changes in the

¹ Reynolds's "System of Medicine," vol. iii. Article, Chronic Pneumonia.

bronchial and alveolar walls, which gradually lead to induration and ulceration of the lung.¹

3. *Pleurisy*.—This, in very exceptional cases, leads to the development of an interstitial pneumonia. It appears to be in those cases of pleurisy which are more or less chronic, and in which the effusion remains long unabsorbed, that such a result is most liable to occur. The induration of the lung thus induced, is often, however, exceedingly partial, consisting merely in some increase of the interlobular connective tissue, originating and extending inwards as dense bands from the thickened visceral pleura. In other cases pleurisy probably gives rise to a much more general fibrosis.

4. *The Inhalation of solid irritating Particles*.—This, which occurs in miners, potters, stonemasons, grinders, etc., is the cause of the fibrosis of the lung so common amongst these workmen. The continuous irritation of the inhaled particles induces a bronchial and alveolar inflammation, and ultimately a progressive fibrosis, with dilatation and ulceration of the bronchi.

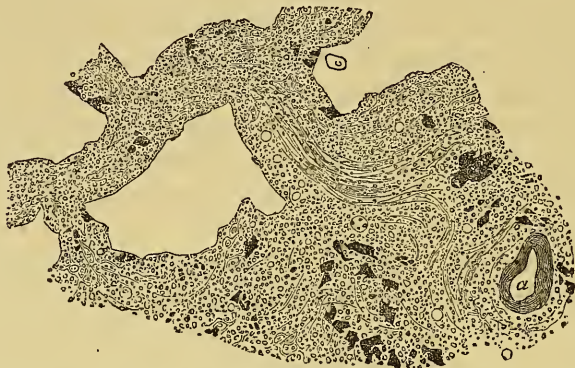
HISTOLOGY, ETC.—The appearances presented by the lung when the fibrosis is extensive and general are very characteristic. The organ is diminished in size; the tissue is smooth, dense, firm—in parts almost cartilaginous in consistence; and it is irregularly mottled with black pigment. The alveolar structure of the lung is in most parts completely destroyed, and on section the dilated bronchi are seen as numerous large openings scattered over its surface. The dilated bronchi frequently become the seats of secondary inflammatory processes, which may lead to ulceration and ultimately to extensive excavation of the indurated tissue; but there is a complete absence of any of those caseous changes which are so characteristic of ordinary phthisis. This secondary inflammation of the dilated bronchi is probably induced by the irritating and often putrid secretion which they contain, and which is only with great difficulty completely removed by expectoration. The pleura is almost invariably considerably thickened and adherent.

The histological changes may be described generally as consisting in the development of a fibro-nucleated tissue from the walls of the alveoli, from those of the bronchi, and from the interlobular connective tissue; which new growth, as it increases, and from its tendency to contract, gradually replaces and obliterates the alveolar structure. The character of these changes, however, varies somewhat according

¹ See case by Dr. Irvine, *Trans. Path. Soc. Lond.*, vol. xxviii. p. 63.

to the inflammatory antecedents in which they originate. When the result of a croupous pneumonia, the primary, and usually the principal,

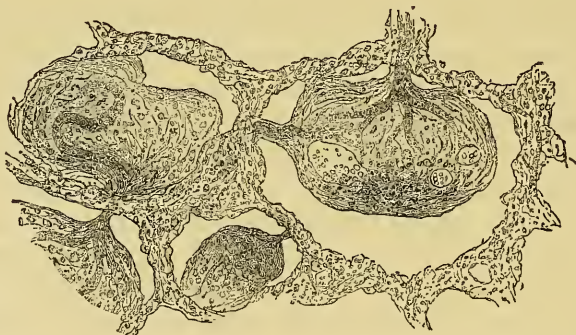
FIG. 130.



Interstitial Pneumonia.—From a case of so-called “cirrhosis” of the lung, in which the disease was unilateral. The bronchi were much dilated, and there was a complete absence of any caseous change. The drawing shows the new fibro-nucleated growth, both in the alveolar walls and in the interlobular tissue, also the pigmentation. At *a*, a divided vessel is seen. $\times 100$.¹

change takes place in the walls of the alveoli (Fig. 130), although ultimately the interlobular tissue is involved. The alveolar walls

FIG. 131.



Chronic Pneumonia.—Vascularization and fibroid development of intra-alveolar exudation products. Bloodvessels are seen distributed in the exudation products, which bloodvessels communicate with those in the alveolar walls. The alveolar walls are also thickened by a fibro-nucleated growth. $\times 100$, and reduced $\frac{1}{2}$.

become thickened by the growth of a small celled-tissue, in which, associated with the lymphoid cells, there are sometimes elongated

¹ When this specimen is examined with a higher magnifying power a delicate reticulum can be seen between the cellular elements.

fusiform cells such as are found in embryonic tissue which is undergoing fibroid development. The new growth in its earlier stages usually contains new bloodvessels, but later the tissue contracts, and these become to a great extent destroyed. The alveolar cavities which are not obliterated, are either empty, or contain exudation products or a few epithelial cells. In addition to the growth in the alveolar walls, I have met with three cases in which intra-alveolar exudation products were undergoing fibroid development.¹ There was nothing peculiar in the macroscopical characters of the lungs, but the alveoli were found filled with a fibrinous meshwork and leucocytes somewhat similar to that met with in red hepatization. (See Fig. 125.) They differed, however, in this respect—that many of the cells were long and spindle-shaped, and bloodvessels were distributed amongst them, which bloodvessels communicated with those in the alveolar walls. (Figs. 131 and 132.) The alveolar walls were also thickened by a fibro-nucleated growth. It was therefore perfectly obvious that in these lungs the products of a previous acute croupous pneumonia were becoming vascularized and undergoing development into a fibroid structure, and that this intra-alveolar change was the principal cause of the fibroid induration of the organs.

When the fibrosis is secondary to an ordinary broncho-pneumonia or to that induced by the inhalation of irritating solid particles, the new growth also originates principally from the alveolar walls. Here, however, the growth in the earlier stages is less uniform, and the peri-bronchial and interlobular connective tissue play a more prominent part in the process.

FIG. 132.



Chronic Pneumonia.—A portion of the intra-alveolar exudation products (Fig. 131) more highly magnified. Showing the elongated spindle cells, the fibrillation, and the bloodvessels containing blood-corpuscles. $\times 200$.

¹ For one of these specimens I am indebted to Dr. Goodhart, who records the case in the *Trans. Path. Soc. Lond.*, vol. xxv. p. 33.

CHAPTER XLVI.

PULMONARY PHTHISIS.

By pulmonary phthisis is understood a disease of the lungs which is characterized by progressive consolidation of the pulmonary texture, and by the subsequent softening and disintegration of much of the consolidated tissue. Respecting the nature of the morbid processes which lead to this consolidation and disintegration of the lungs—various opinions have from time to time been held by pathologists, and this diversity of opinion exists to some extent even at the present day. According to the older views, which were based upon the teaching of Laennec, phthisis was regarded in all cases as a *tuberculous* disease. Tubercle was looked upon as a specific non-inflammatory growth which was characterized by the caseous degeneration which it invariably underwent (see “Acute Tuberculosis”), and this caseous metamorphosis was held to be such a distinguishing peculiarity of the growth, that all caseous masses came to be regarded as tuberculous, and phthisis, in which caseation plays such a prominent part, was consequently regarded as a tuberculous disease. The various consolidations of the pulmonary tissue were described as “infiltrated tubercle,” and tubercle in some form or other was regarded as so essential a constituent of the disease, that “phthisis” and “pulmonary tuberculosis” came to be synonymous terms.

These older views respecting the nature of phthisis have undergone various modifications during recent years. When the application of the term “tubercle” became limited by Virchow and his followers to the gray granulation, it was evident that such views were no longer tenable, and at the present time many, in accordance with the advocacy of the late Professor Niemeyer, regard tubercle as only an occasional element in the causation of the disease. In considering how far tubercle plays a part in the production of phthisis, it must be borne in mind that this growth is now known to be an inflammatory one. The miliary lesions which are commonly known as tubercular, are the anatomical results of chronic inflammatory processes limited to small

circumscribed areas; and although they consist in the main of a small-celled lymphoid tissue, they present certain differences in their histological characters, according to the structure of the organ in which they originate. (See "Acute Tuberculosis.") In the lungs it has been seen that they consist not only of that lymphoid tissue and branched cells which is so characteristic of tubercular lesions, but also of accumulations of epithelium within the pulmonary alveoli. (See "Tuberculosis of the Lungs.")

HISTOLOGY OF PHTHISIS.—The histological changes in the lungs which occur in pulmonary phthisis are similar to those which are met with in these organs in acute miliary tuberculosis. They differ mainly in this respect—that whilst in the latter disease these changes are usually limited to small areas (hence the miliary character of the lesions), in the former they commonly involve much wider tracts of tissue.

In studying pulmonary phthisis, it will be advisable in the first place to describe the various structural changes which are met with in the lungs, together with the more important alterations which they produce in the physical characters of the organs; and subsequently to examine into the nature of the morbid processes upon which these changes depend, and to draw some general conclusions respecting the pathology of the disease.

FIG. 133.



Acute Phthisis.—Showing one of the alveoli filled with epithelial element, and marked cellular infiltration of the alveolar wall. $\times 200$.

The structural changes met with in the lungs in phthisis are mainly of four kinds: 1st. *An accumulation of epithelial cells within the*

pulmonary alveoli ; 2d. *The presence within the alveoli of a fibrinous exudation and leucocytes* ; 3d. *A cellular infiltration and thickening of the alveolar walls, together with, in most cases, a similar change in the walls of the terminal bronchioles* ; and 4th. *An increase in the interlobular connective tissue*. These four kinds of morbid change are very constantly associated, although in very different degrees ; and some of them are more prominent and characteristic than others. The preponderance of one or other of them produces those variations in the physical characters of the lungs which are met with in the different stages, and in the different varieties of the disease. These various structural changes must now be considered separately.

1st. *An accumulation of epithelial cells within the pulmonary alveoli*.—This is one of the most frequent changes met with in phthisis, and is precisely similar to that which has been already described as occurring in cases of true catarrhal pneumonia. (See Fig. 128.) The alveoli are found filled with large nucleated elements, which are

Fig. 134.



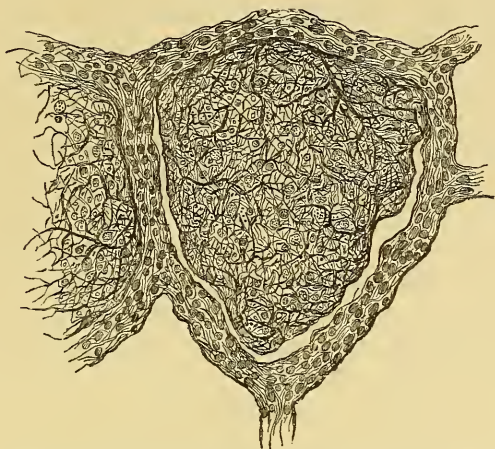
Section of Lung from a Case of Acute Phthisis.—Showing that the consolidation consists almost exclusively of products accumulated *within* the alveoli. In some parts a free space is seen between the alveolar walls and their contents : this is simply due to the shrinking of the latter caused by the hardening of the specimen. $\times 50$.

the offspring of the epithelial cells normally lining the alveolar walls. (Fig. 133.) In some acute cases of phthisis this alveolar accumulation may constitute almost the only morbid change, and although there is always some cellular infiltration of the alveolar walls, the great bulk of the pulmonary consolidation is due to the stuffing of the alveolar cavities with catarrhal products. (Fig. 134.) In some parts—those in which the change is the most recent—the large cells which fill the alveoli and the alveolar walls will be found but little altered, but in the greater portion of the consolidated tissue the cells will be seen in various stages of retrogressive metamorphosis, and the alveolar walls destroyed ; whilst in those tracts of tissue in which the process is most advanced, all trace of structure is

lost, and nothing is seen but a granular *débris*. These changes are precisely analogous to those met with in many of the larger nodular lesions of acute tuberculosis. (See Figs. 86 and 87.)

2d. *The presence within the alveoli of a fibrinous exudation and leucocytes.*—This is less frequent than the preceding. (Fig. 135.)

FIG. 135.



Acute Phthisis.—Showing one of the alveoli filled with fibrinous exudation and leucocytes, and some cellular infiltration of the alveolar wall. $\times 200$.

The exudation products are similar to those which fill the alveoli in ordinary croupous pneumonia. (See Fig. 125.) The coagulum, however, is usually not so abundant, neither is the fibrillation quite so distinct. In the most acute forms of phthisis this may constitute the principal cause of the pulmonary consolidation, but more commonly it is associated with more or less epithelial proliferation.

The appearances presented by the lungs in those cases in which the pulmonary consolidation is mainly due to the *intra-alveolar* changes above described are very characteristic. The consolidated tissue is quite soft and friable, breaking down very readily under the finger, and there is a complete absence of any induration. The consolidation, although frequently almost uniform, sometimes presents a somewhat lobulated outline, indicating the implication of different groups of the pulmonary lobules. The color varies from a reddish to a yellowish-gray and scattered through the consolidated mass are often small portions of a more decidedly yellow tint. These latter correspond with those parts in which the retrogressive changes are the most advanced, and they are even softer in consistence than the surrounding tissue. In many parts the consolidated tissue will be found broken down, so as to form cavities of various sizes. These

always possess irregular walls, which are quite soft and friable, like the solid tissue which surrounds them.

3d. *A cellular infiltration and thickening of the alveolar walls, together with, in most cases, a similar change in the walls of the terminal bronchioles.*—This is very constantly associated with the former intra-alveolar changes, and it must be regarded as the most characteristic phthisical lesion, although its extent varies very considerably in different cases. The change is precisely similar to that which has been already described as occurring in acute miliary tuberculosis. In its earlier stages a few small lymphoid cells are seen infiltrating the alveolar septa, which are thus slightly thickened. (See Figs. 133 and 135.) As the change proceeds, the number of these cells increases, and from them an imperfect fibro-nucleated structure is developed, which in some parts very closely resembles adenoid tissue. (Fig. 136.) This structure contains no new blood-

FIG. 136.



Section of Lung from a Case of somewhat Chronic Phthisis.—Showing the thickening of the alveolar walls by a fibro-nucleated adenoid-like tissue; together with an accumulation of epithelial cells within the alveolar cavity. The latter are undergoing retrogressive changes. $\times 200$.

vessels. As this new tissue develops in the alveolar walls, it gradually obliterates and replaces the alveolar cavities, so that whilst in some portions the thickened alveoli may be found still containing epithelial elements, exudation products, or even giant cells, in others large tracts will be seen, consisting almost entirely of the small-celled growth. The development of this new non-vascular tissue in the alveolar walls leads to the partial, or even complete, obliteration

of the pulmonary capillaries, which, as will be seen subsequently, constitutes an important element in the causation of the retrograde changes.

The changes which may subsequently take place in this alveolar growth vary. The infiltrated septa may rapidly break down before any marked thickening or development of new tissue has had time to occur; whilst in other less acute cases there is a considerable development of the imperfect fibro-nucleated tissue, which, although it may remain as a more or less permanent structure, usually owing to insufficient vascular supply, undergoes in its turn retrogressive metamorphosis. These two kinds of change are very often found taking place simultaneously in different portions of the consolidated lung. In those portions in which the new tissue is undergoing degeneration, it, together with the cells which may be contained within the alveoli, will be seen to have become converted into structureless granular debris, whilst perhaps in immediate vicinity to these more degenerated portions will be found a more permanent fibro-nucleated structure.

Respecting the alteration which the growth of this small-celled tissue produces in the physical characters of the lungs—it may be stated generally, that it usually leads to more or less induration of the pulmonary texture. The extent of this induration, however, will vary according to the characters of the new tissue. If the tissue be almost entirely cellular, such as is the case when it is very rapidly developed, it will produce but little, if any, induration of the pulmonary consolidation, which, consisting mainly of the intra-alveolar accumulations, will be soft and friable in consistence, much resembling that which has been already described. When, on the other hand, as is more frequently the case, there is any considerable development of the imperfect fibro-nucleated growth, or its reticulum is dense and abundant, there will be a corresponding induration of the consolidated tissue. In many cases these changes produce uniform tracts of indurated consolidation of a grayish color mottled with black pigment, in which there may be scattered here and there yellowish patches corresponding to those portions which have undergone retrogressive fatty changes.

4th. *An increase in the interlobular connective tissue.*—This is met with, to a greater or less extent, in all the more chronic forms of phthisis. This tissue, which surrounds the bronchi and bloodvessels, and contributes to the formation of the alveoli, is found not only increased in amount, but also altered in character. In the earlier

stages of its development, when it contains numerous small cells, although many parts of it may resemble the growth in the alveolar walls, its structure is more like that met with as the result of chronic indurative processes in other organs. It has a much greater tendency to become developed into a fibroid tissue than the alveolar growth, and is rarely the seat of those retrograde changes which are so frequent in the tissue originating in the alveolar walls. As usually met with, it consists either of wavy fibres or of a more or less reticulated structure, with a varying number of round, spindle-shaped or branched cells. (Fig. 137.) Associated with it, in most cases, are granules

FIG. 137.



Chronic Phthisis.—Showing the new interlobular fibroid growth surrounding and encapsulating a degenerated and caseous portion of the consolidated lung. $\times 50$, reduced $\frac{1}{2}$.

of black pigment. These differences in the pathological tendencies and structure of the alveolar and interlobular growths are mainly owing to differences in the amount of their vascular supply. Whereas in the former the vessels become obliterated in the manner already described, in the latter this obliteration is much less complete or entirely wanting. In the most chronic cases of phthisis this interlobular growth may constitute the predominant structural change, and large tracts of the pulmonary texture may be found completely replaced by it. (See “Interstitial Pneumonia.”)

An increase in the interlobular connective tissue in phthisis—in-

much as the new tissue has so marked a tendency to become dense and fibroid—leads to extensive induration of the pulmonary texture; and further, owing to the contraction which the tissue tends to undergo, its growth ultimately produces a corresponding contraction of the diseased lung. In all those cases of phthisis in which there is either a marked thickening of the alveolar walls, or an increase in the interlobular connective tissue, any cavities which may exist in the consolidated and indurated tissue are characterized by the tough and fibroid character of their walls, these presenting a marked contrast to the soft friable tissue which surrounds the cavities in those cases in which the pulmonary consolidation is mainly due to intra-alveolar changes.

Changes in the Bronchi.—Allusion must now be made to certain changes in the bronchi. These tubes are invariably more or less involved in pulmonary phthisis. Some catarrh of the bronchi is constantly present in phthisical lungs. The catarrh is sometimes general, but much more commonly it is limited, and more strictly confined to such portions of the lung as are becoming, or have already become, consolidated. In many cases there is a marked tendency of this bronchial catarrh to lead to extensive cellular infiltration of the deeper structures of the bronchial wall. This is especially the case in the scrofulous. (See “Scrofulous Inflammation,” Fig. 76.) This cellular infiltration sometimes leads to the production of small ulcers. These have thickened opaque edges, and when once formed they tend to increase. In addition to these changes in the bronchial mucous membrane, there is often a cellular infiltration of the peri-bronchial tissue, and here small nodules of new growth are frequently met with—especially around the smallest bronchi. The development of these nodules is probably due to the transmission of infective substances by means of the lymphatics from the bronchial mucous membrane (tuberculosis).

PATHOLOGY OF PHTHISIS.—Having thus briefly described the various structural changes met with in the lungs in phthisis, it remains to consider the nature of the morbid processes upon which they depend. In the first place, it is evident that these changes are analogous to those which have been seen to occur in the several forms of pulmonary inflammation. The fibrinous exudation and leucocytes, and the accumulation of epithelial cells within the alveoli in croupous and catarrhal pneumonia, with, in the more chronic cases, the ultimate infiltration of the alveolar walls; and the increase in the interlobular

connective tissue which characterizes the interstitial process, closely resemble the phthisical lesions. These considerations, together with those derived from the study of the etiology of the disease, are sufficient to justify the conclusion that the morbid processes which lead to the consolidation and subsequent disintegration of the lung come within the category of *inflammation*, and that the differences in the histological changes to which they give rise are mainly due to differences in the intensity, in the duration, and in the mode of origin of the inflammatory process.

In considering the causes of these differences in the histological changes in the lungs, it is important to bear in mind what has been already stated respecting the variations in the character of the textural alterations in inflammation which are produced by differences in the intensity and duration of the inflammatory process. (See "Varieties of Inflammation.") When studying the process of inflammation it was seen that the most intense forms of the process were characterized by abundant fibrinous exudation and emigration; whereas in inflammations of less intensity the textural changes played a more prominent part. These textural changes also varied according to the intensity of the inflammation. In the least severe and most chronic forms these changes tended to be limited to the elements immediately adjacent to the bloodvessels and lymphatics, whereas in inflammations of somewhat greater intensity more distant elements became involved. Further, whereas in the former case these changes usually resulted in the formation of a small-celled tissue which tended to become fibroid, in the latter, the more distant elements—being in most cases incapable of further development—tended to undergo retrogressive changes. In the lungs, the truth of these propositions was borne out by the differences which were seen to exist in the histological characters of the lesions in the various forms of pulmonary inflammation, and also in acute tuberculosis.

If the pathology of these inflammatory processes in the lungs be kept in view, the explanation of the differences in the histological characters of the lesions in pulmonary phthisis becomes tolerably evident. In those cases in which the inflammatory processes are of slight intensity and of long duration, the most marked structural change will consist in the development of a small-celled growth in the alveolar walls and in the interlobular tissue—a growth which tends, more or less, to become developed into a fibroid structure; whereas in those cases in which the inflammation is of greater inten-

sity, fibrinous exudation and emigration, and proliferation of the alveolar epithelium, will constitute more prominent parts of the process.

The intensity of the inflammatory process not only determines to a great extent the histological characters of the pulmonary consolidation, but also the subsequent changes which take place in it. In those cases of phthisis in which the intensity of the inflammatory process is considerable, not only do the epithelium and exudation products which have accumulated within the alveoli quickly degenerate and break down, but any small-celled tissue which may have been developed in the alveolar walls or around the terminal bronchioles also softens and dies, and thus the vitality of large tracts of the pulmonary consolidation may become destroyed. In those cases, on the other hand, in which the process is less intense, the small-celled growth produced in the alveolar and bronchial walls is more permanent, and there is an increase in the interlobular connective tissue. It is these two kinds of change, the one tending towards death, and the other towards progressive development, which produce the caseation and softening on the one hand, and the induration on the other, which, associated in such various degrees, make up the diverse physical characters of the phthisical lung.

These various secondary changes which may take place in the pulmonary consolidation of phthisis must be considered more fully. They are of three kinds—resolution, development into an imperfect fibroid tissue, and retrograde metamorphosis.

Resolution.—Much of that consolidation of the lung which is the most rapidly induced, and which is consequently owing to the presence of intra-alveolar exudation matter, may become absorbed. The resolution of the consolidation may thus be complete, or after the absorption of the intra-alveolar products there may remain more or less infiltration of the alveolar walls.

Fibroid Development.—This, as has been seen, may take place in the growth in the alveolar walls, and also in the new interlobular tissue. The tissue which originates in the walls of the alveoli, however, being for the most part destitute of bloodvessels, is incapable of forming a very mature structure, although it may become developed into an imperfect adenoid-like tissue, which may remain for some time permanent, and so contribute to the induration of the lung. In the new interlobular tissue, there is not the same interference with the vascular supply, and hence this forms a much more fully developed and permanent structure, and it is the principal source of the pulmo-

nary fibrosis. The extent of this fibrosis is, for the most part, in direct proportion to the chronicity of the disease.

Retrograde Metamorphosis.—It is this kind of change which leads to that caseation, softening, and disintegration which is so characteristic of phthisis, and which distinguishes phthisical from other forms of pneumonic consolidation. A retrograde change in the inflammatory products is an invariable accompaniment of acute non-phthisical pneumonia. Much of the exudation matter and epithelium which fill the alveoli undergoes fatty and mucoid changes, and as the circulation becomes restored in the pulmonary capillaries, the degenerated products are absorbed, and the lung remains intact. In phthisical consolidation, however, this removal of the inflammatory products does not take place. The contents of the alveoli degenerate, but the degenerated products are not absorbed, and the consolidated lung undergoes a rapid or gradual process of disintegration.

In studying the causes of this retrograde metamorphosis, which constitutes so essential a feature of the disease, it is undoubtedly principally due to conditions interfering with the circulation. Of these conditions, that which occupies the most prominent place is that cellular infiltration of the walls of the alveoli and smaller bronchi which is such a constant though very variable factor in phthisis. It has been seen that this infiltration is especially characteristic of scrofulous inflammations, and that it occurs in a modified form in those who are not markedly scrofulous, and also in all pulmonary inflammations which become chronic. When the infiltration is marked, and especially when rapidly induced, the effect of the pressure which the young cells exercise upon the pulmonary capillaries is to obstruct the circulation, and so not only to prevent the absorption of any intra-alveolar products, but also to lead to necrotic changes.

There are two other conditions which, although of less importance than the preceding, also tend to interfere with the circulation, and so to cause necrosis. These are the pressure which is exercised upon the pulmonary capillaries by the inflammatory products which have accumulated within the alveoli; and that tendency to stagnation of the blood-stream which is an invariable accompaniment of every intense inflammation. The operation of these conditions obtains in the most acute forms of phthisis.

In addition to the interference with the circulation, an important element in the causation of the retrograde changes of phthisis is probably that inherent weakness of the lungs (usually inherited),

which not only renders them especially susceptible to injury, but also, when injured, renders them abnormally incapable of recovering themselves from the inflammatory process which has been induced.

In many cases of phthisis also, especially in the more chronic forms, secondary inflammation and ulceration of the pulmonary consolidation, resulting from the injurious influence of retained secretions and inflammatory products, constitutes an important factor in the causation of the destruction of the lung.

ETIOLOGY OF PHTHISIS.—In studying the etiology of phthisis it will be necessary to consider, in the first place, that inherent pulmonary weakness which exists so frequently in this disease; secondly, to examine into the several methods by which injuries may be inflicted on the lung in such a way as to set up an inflammatory process; and lastly, to point out in what way the occurrence and progress of the disease are influenced by the general health of the individual.

Inherent pulmonary weakness, usually inherited but often acquired, exists in a large proportion of the cases of phthisis. This weakness not only renders the lungs abnormally susceptible to the various kinds of injurious irritation, but also makes them less capable than strong lungs of recovering themselves from the effects of the inflammatory process which the injury has produced. Inherent pulmonary weakness is most frequently, but by no means always, a part of that general constitutional state known as scrofula, in which the mucous membranes generally, and especially that of the respiratory organs, are so abnormally liable to become inflamed.

Inflammatory processes may be induced in the lungs by—1st, injuries inflicted upon the surface of the body; 2d, by injuries inflicted through the medium of the bronchi; and 3d, by infection.

By injuries inflicted upon the surface of the body I mean that general chilling of the surface which results from exposure to cold. That this is a frequent cause of bronchial and pulmonary inflammation is well known.

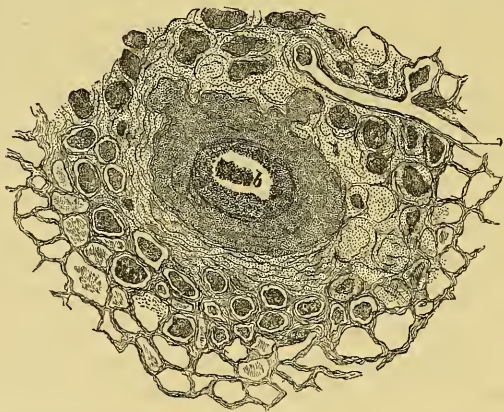
A more important agent in the production of phthisis than the preceding is the injurious irritation of the lungs through the medium of the bronchi. The bronchial mucous membrane, communicating as it does with the external air, is especially liable to injury, and the extreme frequency with which the development of phthisis is preceded or accompanied by successive attacks of bronchial catarrh is a well established clinical fact, the important bearing of which upon the

successful treatment of the disease it would be difficult to over-estimate. In considering bronchial catarrh as a cause of phthisis, it is important to bear in mind how greatly the occurrence and character of this catarrh are influenced by the existence of scrofula.

In other cases, injuries inflicted through the medium of the bronchi appear to exercise their influence directly upon the inner surface of the air-vesicles without producing any inflammation of the bronchial mucous membrane. This is probably a very important way in which such injuries cause phthisical consolidation of the lung.

The prominent position which these injuries inflicted through the medium of the bronchi occupies in the causation of phthisis, is shown by the fact that the lung-consolidation in this disease is, for the most part, *lobulated* in its distribution. Groups of air-vesicles communicating with the terminal bronchioles become implicated, and thus are produced lobular lesions. (Fig. 138.) This lobulated distribution

FIG. 138.



Acute Phthisis.—A transverse section of a terminal bronchus (air-passage) and the surrounding alveoli.—Showing the lobulated character of the pulmonary consolidation. *b*, cavity of bronchus containing a little mucus. *v*, a blood vessel. $\times 50$, reduced $\frac{1}{2}$.

of the phthisical consolidation is exceedingly characteristic, and even in those acute cases, in which, owing to the rapid and extensive implication of the lung, the consolidation may to the naked eye appear almost uniform (like a croupous pneumonia), the microscope will usually reveal a lobular character.

The last method by which injuries may be inflicted upon the lungs is by means of infection. By this is understood the property possessed by certain inflammatory products—especially by those which have become caseous—of exercising an injurious influence upon the immediately adjacent, and also upon distant tissues, and so leading to the development of secondary inflammations. (See “Infective Inflammations.”) Phthisical consolidation of the lung frequently possesses, to a greater or less extent, this infective property, as a consequence of which the consolidation tends to spread and involve larger areas of the pulmonary tissue; and also, owing to the absorption and dissemination of infective particles, it tends to cause secondary inflammatory processes in its vicinity or in more distant parts. This infective property is precisely similar to that which has been seen to exist in the focus of infection in acute tuberculosis; but whereas in this disease the dissemination of the infective particles takes place by means of the bloodvessels, in the more limited processes which occur in phthisis it is effected principally by the lymphatic vessels and serous canals. It is this more limited infection which gives rise to many of the nodules of induration which are so frequently met with in phthisical lungs. The infective process usually supervenes upon pre-existing phthisis.

There remains still one other factor which has a most important influence upon the causation of phthisis—the *general health of the individual*. That the development and progress of phthisis is greatly influenced by the state of the general health is well known. That this should be so, will be readily understood if the inflammatory nature of the disease be kept in view, inasmuch as, in all cases, the susceptibility of a living tissue to injury is, *cæteris paribus*, greater, and the power of recovering itself from the effect of the inflammation less, the lower the standard of the general health.

VARIETIES OF PHTHISIS.—In conclusion, allusion must be made to the different varieties of pulmonary phthisis. How far is a subdivision of the disease into different *pathological* varieties admissible? Although the variations observed in the physical characters of phthisical lungs and also in the clinical history of the disease, have led to its subdivision into different kinds, it appears to me that there are no pathological grounds for any such subdivision. The variations observed in the clinical history of phthisis and in the physical characters of phthisical lungs are, I think, mainly to be ascribed to variations

in the duration and intensity of the inflammatory processes which give rise to the pulmonary consolidation, and also to the parts which primary pulmonary inflammation, bronchial inflammation, and infection, play respectively in the causation of the disease.¹

CHAPTER XLVII.

THE PREPARATION AND MOUNTING OF SPECIMENS.

IN this, the concluding chapter, it is proposed to describe very briefly the more common methods of preparing and mounting specimens for microscopical examination. It is not intended to give an account of those various and complex methods of investigation which are required for minute histological research, but merely to describe those more easy ones which suffice in the great majority of cases for the recognition of the structural alterations met with in disease. In order to be as brief as possible, those methods only will be described which I believe to be the most readily available and at the same time to yield the most satisfactory results. The subject will be treated under the following heads: 1st. *The Examination of Specimens whilst fresh*; 2d. *The Hardening of Specimens*; 3d. *The Making of Sections*; 4th. *Staining*; 5th *Preservation and Mounting*.

The Examination of Specimens whilst Fresh.

Very much may be learnt from the examination of specimens in their fresh state before they have been submitted to any hardening process. The examination may be conducted either by making thin sections of the tissue with a Valentin's knife, or by cutting off a minute portion and tearing it to pieces with fine needles. The specimen prepared in either of these ways may be examined in a .75 per cent. solution of chloride of sodium, or in glycerine. Thin membranous structures may be examined by simply spreading them out in a drop

¹ For a more complete account of Pulmonary Phthisis, see—"The Pathology of Pulmonary Consumption," by the Author, 1878.

of water placed upon the glass slide, and then covering them with glycerine.

The method of making sections of organs whilst fresh with a Valentin's knife is an exceedingly easy and useful way of at once ascertaining in the post-mortem room the existence of the more marked structural changes. The knife should be well wetted with water, and then drawn *rapidly* through the substance of the organ. The section thus obtained is gently washed in water before being examined in saline solution or glycerine. A rough examination of the liver, kidneys, and lungs is in this way readily made.

The muscular fibres of the heart and tumors may be examined by the process of teasing. This process, however, is usually more readily effected after the specimen has been kept in Müller's fluid or in a solution of bichromate of potash in the manner to be hereafter described. In the examination of tumors, much may be learnt by gently scraping the freshly-cut surface with a knife and examining in glycerine the elements which are thus separated.

The Hardening of Specimens.

In order to make a complete and satisfactory examination of diseased structures, it is in almost all cases necessary to submit them to a process of hardening. By this process they are so altered that fine sections of them can be made, and the sections are also rendered more fit for permanent preservation than are those obtained from tissues in their fresh state. Numerous substances have been employed as hardening agents. Those, however, which are the most generally valuable are *Müller's fluid*, *chromic acid*, *bichromate of potash*, and *alcohol*.

Müller's Fluid.—Of all hardening agents this is the most satisfactory and the one most generally applicable. It is prepared in the following way:—

Take of—

Potassium Bichromate	2 parts.
Sodium Sulphate	1 part.
Water	100 parts.
Dissolve.	

The tissue should be kept in this solution for from one to two weeks, and then placed in common alcohol for two or three days, after which it is ready for making sections.

The advantages of Müller's fluid are that it alters the macroscopical characters of tissues less than other hardening agents, and its penetrating powers are so great that it is not necessary to cut the tissue up into small pieces, but the whole organ may be placed in it. The tissue may be kept in it longer without injury than in other aqueous solutions.

Müller's fluid is also valuable for the maceration of tissues which are to be examined by teasing—as tumors, muscle, etc. Its action tends to facilitate the isolation of the elements.

Chromic Acid.—This is less generally applicable than the preceding. It should be used in aqueous solution—strength one-sixth per cent. It is important to employ the solution in large quantities—from six to ten fluidounces for each specimen. The tissue must be cut with a sharp razor into small pieces—not much larger than a hazel-nut—before it is placed in the solution. The hardening is usually completed in from five to eight days. It is hastened by renewing the solution. If kept too long in the solution the tissue becomes brittle. All tissues which have been hardened in chromic acid should be placed in common alcohol for about twenty-four hours before sections are made. Chromic acid is preferable for hardening skin and mucous membranes.

Bichromate of Potash.—This agent is more gradual in its action than chromic acid, and produces less shrinking of the tissue. It is especially valuable for the hardening of kidney, bloodvessels, nerve-tissue, ovary, and some other structures. It is often advisable to commence the hardening with bichromate of potash, and then to complete it in chromic acid or common alcohol. The bichromate is also valuable for the maceration of tissues which are to be examined by teasing. The bichromate should be used in aqueous solution—strength about two per cent. It penetrates more readily than the chromic acid, and consequently it is not necessary to use quite such small pieces of the tissue. The tissue must be kept in the solution from two to three weeks, the solution being changed every four days.

Alcohol.—This is most valuable as an agent for the completion of the hardening of tissues which have been previously placed in Müller's fluid, chromic acid, or in bichromate of potash. The tissues should be kept in it one or two days. Some tissues, however, appear to harden better if they are at once placed in alcohol; amongst these are the lymphatic glands, spleen, and testis. Common (methylic) alcohol answers for all these purposes. Lastly, alcohol must be employed

for the hardening of all tissues which have been injected. Absolute alcohol is often necessary for the completion of hardening of many tissues.

The Softening of Tissues.—Some tissues, as osseous structures, tumors which have become calcified, etc., require to be softened before sections can be made. This may be effected by placing them in the one-sixth per cent. chromic acid solution, to each six ounces of which three or more drops of concentrated hydrochloric acid have been added.

The Making of Sections.

Although various instruments have been contrived for making sections, the one which answers best is a common razor, or a similar blade firmly fixed in a wooden handle. The usefulness of this instrument is much increased if the lower surface of the blade be ground perfectly flat, whilst the upper is made slightly concave.

Hardened tissues from which sections are to be made must always have first been placed in common alcohol, in the manner already described. In making the section the blade of the instrument must be kept well wet with common alcohol, and the section when cut must be placed at once in the same liquid.

Imbedding.—Hardened tissues which are too small or too delicate to be held in the hand for the purpose of making sections, must be imbedded. The object of imbedding is to fix the tissue in some substance which can not only be readily held, but which can also be easily cut with the section-knife. Various substances are used for this purpose. Of these the one which is most generally applicable is a mixture of white wax and olive oil. Equal quantities of pure white wax and olive oil should be warmed together and well mixed, and the mass when cold may be kept and used as required. When a specimen is to be imbedded, a small case of paper should be made somewhat larger than the specimen. The edges of the paper can be secured with a little mucilage or with a pin. The mixture of wax and oil is then melted and the paper case filled with it. The specimen to be imbedded—which must have been removed from the common alcohol—is now to be slightly dried on blotting-paper and immersed in the melted compound. The process of immersion requires a little care. The specimen should be placed upon the point of a fine needle, and as soon as the wax commences to solidify at the sides of the case, it

must be dipped beneath the melted liquid so as to be completely covered by it. The needle must then be removed by giving it a gentle twist so as not to disturb the specimen. When the wax is cool the paper can be removed and the mass placed in common alcohol. Sections can be made from it when convenient.

Staining.

When the section has been made and placed in common alcohol, in the manner described, it is usually advisable to stain it. The object of staining is to impart to the different portions of the tissue different shades of color, so that its structure can be more readily recognized. The substances which are the most generally applicable for this purpose are *logwood* and *carmine*. Of these, logwood is the preferable, inasmuch as it is not only differentiates most tissues more completely, but it is a much more agreeable color to work with.

Staining with Logwood.—The following is the method for preparing the logwood solution recommended by Dr. Klein:—

Take of—

Extract. Hæmatox. 6 grammes.

Alumen 18 grammes.

Mix thoroughly in a mortar.

Add gradually whilst stirring—

Distilled Water 28 cub. cent.

Filter.

To the filtrate add—

Spirit. Rect. 1 drachm.

The solution must be kept in a stoppered bottle for a few days before being used.

For staining, several (5–10) drops are to be added to half a watch-glass of distilled water. The thus diluted solution should be filtered before being used. Sections which have been removed from common alcohol are to be placed in the dilute solution for from ten to twenty minutes, and then to be washed in distilled water.

Gradual Staining with Weak Carmine.—In staining with carmine two methods may be employed: the one consists in using a strong solution, so as to stain rapidly; the other in staining very gradually with a much less concentrated liquid. Of these, the method of gradual staining with weak solutions yields the most satisfactory results,

inasmuch as by this means the differentiation of the tissue is rendered more complete than when the coloration is rapidly induced. The process of rapid staining with strong carmine is, however, the most convenient, and it yields, in most cases, sufficiently satisfactory results.

The following is the method for gradual staining recommended by Dr. Klein:—

Take of—

Powdered Carmine. 2 grammes.

Rub it up with a few drops of Distilled Water.

Add—

Liquor Ammoniaë fort. 4 cub. cent.

Distilled Water. 48 cub. cent.

Mix together with a glass rod, and filter.

The solution to be kept in a stoppered bottle.

For staining, take one drop of the above solution, and add to it from nine to twelve drops of distilled water. Sections, which have been removed from common alcohol, to be placed in this from sixteen to twenty-four hours.

Rapid Staining with Strong Carmine.—To stain rapidly, the sections may be placed in the above strong solution of carmine without the addition of water. In this case the strong solution of carmine should have been kept exposed to the air for a sufficient length of time to allow the excess of ammonia to escape. It is consequently advisable to have two bottles of strong carmine solution—one for rapid, and the other for gradual staining.

The time required for rapid staining is from thirty seconds to five minutes. This, however, will vary very considerably according to the nature of the tissue to be stained. A knowledge of the amount of time which yields the best results will be readily learnt by a little practice.

The sections when removed from the carmine staining solution must be washed for a few seconds in distilled water containing one-quarter per cent. of acetic acid.

Preservation and Mounting.

When the section has been stained, it is ready to be prepared for mounting permanently. The two substances in which tissues are

most commonly mounted are glycerine and Dammar varnish. Of these, the latter should be employed in all cases in which the preservation of the section is intended to be permanent. Many tissues, however, yield more satisfactory results when examined in glycerine; but they cannot be preserved in this liquid for any great length of time without undergoing some alteration.

The methods of mounting in Dammar varnish and glycerine must be described separately.

Mounting in Dammar Varnish.—When the section is to be mounted in Dammar—it having been already stained and washed—it must first be placed in *absolute* alcohol for about a quarter of an hour. From the alcohol it must be transferred to oil of cloves, the superfluous alcohol having been first removed from the section by blotting-paper. In the oil of cloves it becomes, in a few seconds, quite transparent. The superfluous oil must be removed by blotting-paper, and the section is then ready for mounting in the Dammar varnish. If more convenient, it may be kept for one or two days in the oil of cloves before it is mounted in the Dammar. In order to make the specimen still more secure, a layer of the varnish may be placed round the edge of the covering glass a few days after the section has been mounted.

The following is the method of preparing the Dammar varnish:—

Take of—

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